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CONTENTS

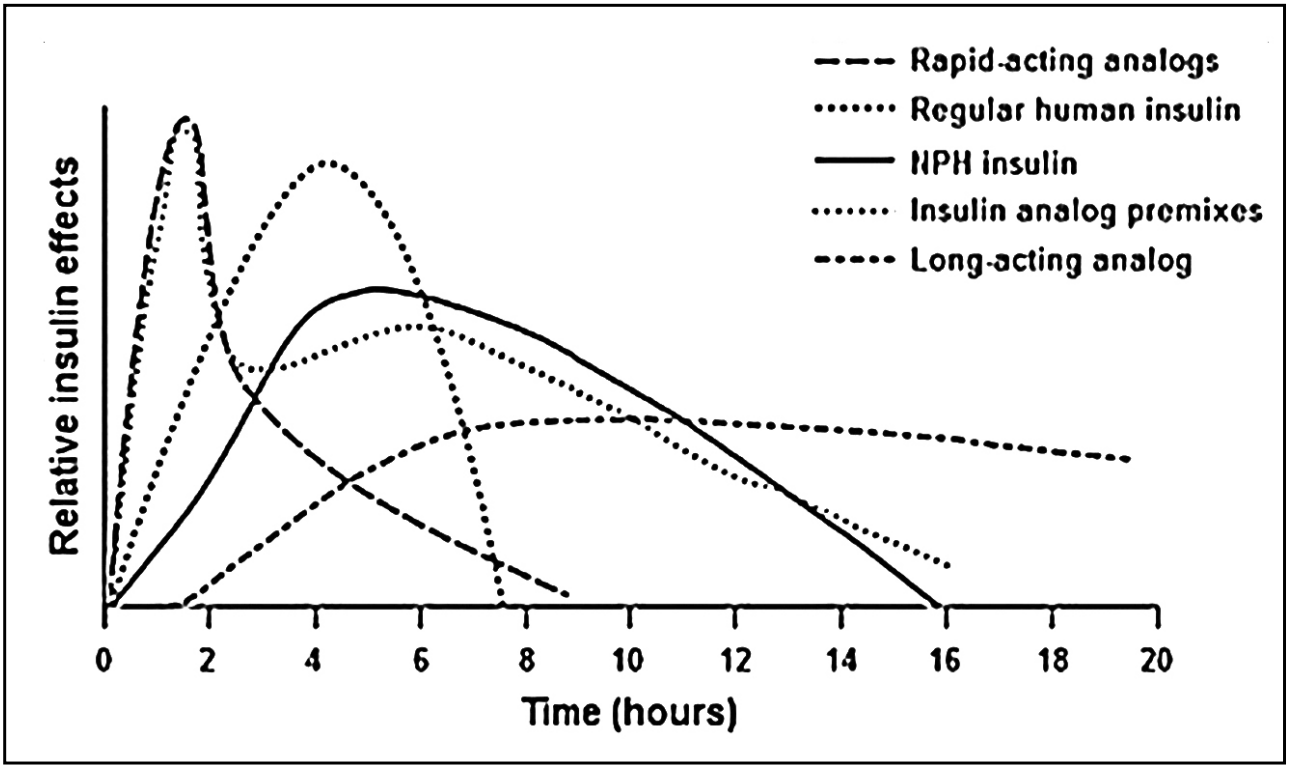
SAFE REGIMENS OF INSULIN THERAPY

Vijay Negalur*

Global estimates show a rising incidence of Type 2 diabetes mellitus (T2DM), resulting in about 90% of cases by the obesity, pandemic and an aging population. In Type 1 diabetes mellitus (T1DM), which is characterized by a complete lack of endogenous insulin, insulin regimen is proven to be lifesaving. The disease progression of T2DM is not clearly understood. It is characterized by insulin resistance and slowly progressive β-cell failure. Although other classes of glucose-lowering medications can frequently achieve glycemic control after diagnosis, a considerable number of people will still require insulin therapy to meet optimal blood glucose targets. There is significant clinical inertia with insulin initiation, especially in people with T2DM, despite evidence-based consensus guidelines and the demonstrated benefits of effective glycemic control. Fear of hypoglycemia, risk of weight gain, restriction of lifestyle, unwillingness to inject and challenges with self-managing insulin therapy are important factors that have an impact on insulin therapy. Consequently, less rigorous insulin regimes with a decreased risk of hypoglycemia are required. Insulin regimens differ in their glycemic efficacy, complexity, risk of hypoglycemia and weight gain and may require subsequent intensification. Furthermore, the education and empowerment of individuals to self-manage their insulin regimen is of vital importance. Figure 1 shows the time-action profiles of insulin preparations.

Figure 1

Time-action profiles of insulin preparations



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TYPES OF INSULIN REGIMENS IN T1DM

- Multiple dose injection (MDI) or basal-bolus therapy
- Continuous subcutaneous insulin infusion (CSII)
- Twice-daily premixed insulin regimen

Many patients still find using insulin analog in basal-bolus regimens to be an excellent choice and studies have shown that this increases patient treatment satisfaction. CSII (insulin pump) therapy shows higher glycemic effectiveness compared to a basal-bolus regimen, with a considerable reduction in severe hypoglycemia. However, it may not completely prevent mild-to-moderate hypoglycemic episodes. Studies measuring the CSII's cost-effectiveness have found that it offers fair value for money. Although, early intensification of insulin therapy should be encouraged, a twice-daily premixed insulin regimen is a potential option for people with T1DM because it is straightforward, simple for caregivers to adopt and may be helpful for people who struggle to comply with MDI or CSII therapy. However, in a 10-year follow-up study of insulin regimens conducted among 7206 children and adolescents with T1DM attending summer camps, Redon et al. found that premixed regimens were the least favoured for use and did not exhibit glycemic superiority compared to other intensive insulin therapies.

For a long time, until the advent and development of CSII using insulin pumps, basal-bolus therapy which is a well-established intensive therapy, was the best therapeutic option for patients with T1DM. An insulin pump mimics the physiological situation by providing extra bolus doses to meet prandial insulin requirements and a continuous insulin infusion rate to meet basal insulin requirements. Until now, several randomized clinical trials (RCTs) have indicated that CSII leads to lower HbA1c levels than MDI. In real-world data analysis, Guo Keyu et al. demonstrated that patients who underwent CSII therapy, compared with those who received MDI therapy had lower levels of HbA1c and fasting blood glucose (FBG). Moreover, CSII therapy was associated with better glycemic outcomes in terms of increasing time in range (TIR), decreasing time above range (TAR) and achieving (Continuous Glucose Monitoring) CGM-associated targets of TIR ≥70% and TAR <25%. Several meta-analysis showed that CSII does not increase the risk of adverse events (maybe with the exception of diabetic ketoacidosis) and there is also a reduction in the incidence of hypoglycemia with the insulin pump use compared to MDI.

CSII is superior to multi-dose injections in lowering blood sugar levels. Careful individual consideration, education and support are necessary for its optimal use.

TYPES OF INSULIN REGIMENS IN T2DM

1) Basal-only regimen

A 'basal-only regimen' involves adding long-acting or intermediate-acting insulin to OHAs or non-insulin injectables such as glucose-like peptide-1 receptor agonists (GLP-1 RA). It is commonly recommended when glycemic targets are difficult to achieve despite the intensification of oral drug therapy. A basal regimen is straightforward, easy to initiate, associated with fewer hypoglycemic episodes and less weight gain compared with more complex insulin regimens which require two or more insulin injections a day. The general guidelines involve administering injections once or twice a day, beginning at a low dose and titrating insulin according to the patient's needs in order to achieve specific control of FBG.

2) Twice-daily premixed insulin regimen

A premixed insulin regimen is commonly employed as a treatment intensification measure in individuals with T2DM failing to achieve HbA1c targets despite a 'basal insulin add-on to a oral anti-diabetes drugs (OADs)' regimen. The rationale for choosing twice-daily premixed insulin over a basal insulin regimen to intensify therapy in OAD failure may be influenced by a

higher baseline HbA1c (>9.5%) and/or the dominance of post-prandial hyperglycemia with most fasting glucose readings closer to target. A drawback of biphasic regimens is the lack of flexibility in insulin dose titration between long-acting and short-acting components, higher rates of hypoglycemia, weight gain and also increased rates of adverse events that may preclude their regular use for elderly individuals. A premixed insulin analog regimen has a superior advantage over biphasic human insulin in terms of improved glycemic control, fewer hypoglycemic events and lower treatment discontinuation rates.

3) Basal-bolus regimen

People with an active lifestyle and unpredictable eating patterns are best suited for a basal-bolus intensive regimen which necessitates regular blood glucose monitoring. The 4-T study was a three-year randomized trial that was carried out to determine the best starting insulin regimen for 708 people with poorly controlled T2DM. Study subjects were randomized to biphasic insulin apart twice daily, prandial insulin a part three times daily or basal insulin detemir once daily (twice if required). Compared to premix and prandial insulin regimens, a basal insulin regimen was linked to fewer hypoglycemic episodes and reduced weight gain. Importantly, without experiencing additional hypoglycemia or weight gain, two-thirds of participants in the basal or prandial groups who underwent treatment intensification to adopt a basal-prandial regimen achieved an HbA1c target of 7% (OR 1.75; 95% CI 1.11 to 2.77).

There are pros and cons of twice-daily premixed insulin doses versus basal-bolus therapy. The perceived burden of extra injections and glucose self-monitoring is associated with the basal-bolus regimen. However, these regimens might provide benefits associated with a more physiological intra-day glucose profile which could offset the burden of the regimen. On the other hand, premixed inulin has fewer injections and is easy to use. Research indicates that T1DM and T2DM patients place importance on ease of use, convenience, social comfort and flexibility of the treatment regimen for insulin administration. A study by Marcia-et al. found that in T1DM and T2DM, a basal-bolus insulin regimen is more effective than twice-daily premixed insulin in terms of glycemic control, treatment satisfaction and quality of life (QoL). In this trial, the rates of hypoglycemia were similar in both groups and the dropout rate was considerably lower in the basal-bolus group. Figure 2 shows insulin regimens in T2DM.

INSULIN INTENSIFICATION

Insulin intensification includes adding mealtime bolus doses, increasing the frequency of administration and/or moving from basal insulin to premixed insulin. The relentless, progressive nature of T2DM results in an almost inevitable need for insulin supplementation and its intensification in an attempt to combat a worsening glycemic profile, including glycemic variability and the associated increased risk of vascular complications. Basal insulin provides an effective method for initiating insulin therapy in people with T2DM, resulting in significant improvements in glycemic control, lower rates of hypoglycemia and less weight gain than either prandial or premixed insulin regimens. However, the inability of basal insulin to correct excessive post-prandial glucose (PPG) excursions means that insulin therapy will eventually need to be intensified. The prandial insulin may be administered initially prior to the meal causing the greatest glucose excursion and further mealtime doses may be added as needed. According to some research, premixed insulin may result in larger reductions in HbA1c compared to basal insulin

Figure 2
Insulin Regimens in Type 2 Diabetes Mellitus

Insulin regimen	Choice of insulin	Duration of action: Onset	Peak	Duration	Initiation	Titration	Indication for change	Other comments
Basal-only insulin regimen	Basal or intermediate acting human insulin, eg, Insulatard, Insuman basal, Humulin I	2–4 h	4–8 h	14–16 h	Usual start is 10 units or 0.1–0.2 units/kg	▶ Patient-led titration by 2 units at approximately three day intervals aiming for target FPG of 5.5–6 mmol/L without nocturnal hypoglycaemia ▶ Reduce the dose by at least 2–4 units or 20%, whichever is greater if FPG falls <4 or unexplained hypoglycaemia	▶ Suboptimal HbA1c targets or fasting blood glucose or both ▶ Fasting glucose levels at target but postprandial glucose levels remain high despite maximum tolerated OHAs ▶ Recurrent and/or unresolving hypoglycaemia and/or nocturnal hypoglycaemia	▶ Simple and easy to initiate with a lower risk of hypoglycaemia and weight gain ▶ Compared to human basal insulin, analogues offer advantage of lower rates of nocturnal hypoglycaemia ▶ Continue OHAs at current doses unless contraindicated or not tolerated
	Long-acting analogues, eg, glargine (Lantus), Levemir (Detemir)	1–4 h	None	Up to 24 h				
	Newer long-acting analogues*, eg, Tresiba (Degludec), glargine U300† (Tougeo)	30–90 h	None	Up to 42 h				
The three newer classes of glucose-lowering agents that is, DPP-4 inhibitors, GLP-1 agonists and sodium glucose co-transporter-2 inhibitors all have licence to use in combination with insulin and can be useful in select individuals if not already considered in the treatment paradigm prior to intensification to basal-bolus regimen or pre-mix insulin regimen[60]								
Premixed twice-daily insulin regimen	Pre-mixed or biphasic human insulins, eg, Humulin M3 (30% short-acting insulin with 70% intermediate-acting insulin), Insuman comb 15, 25 or 50	30 min	2–8 h	Up to 24 h	Usual start is 10 units twice daily (consider lower dose in frail, elderly or 'slim' individuals)	▶ Titrate morning dose by 2 units or 10% increments against target blood glucose of <6 mmol/L before lunch and before evening meal ▶ Titrate evening dose by 2 units or 10% increments against target blood glucose of 6–8 mmol/L before bed and 5.5–6 mmol/L before breakfast	▶ Suboptimal HbA1c targets or FPG or both ▶ If pre-evening meal blood glucose are high and further increase in morning dose results in mid-morning hypoglycaemia ▶ Patient preference or lack of flexibility with regimen	▶ Simple and easy to initiate ▶ Effective in addressing both fasting and prandial glycaemia ▶ Preferred for initiation when HbA1c >9.5% ▶ Higher risk of hypoglycaemia (may preclude regular use in certain groups, eg, elderly) and weight gain
	Pre-mixed or biphasic analogue insulin, eg, Humalog Mix 25 (25% lispro and 75% neutral protamine lispro), Novomix 30 (30% aspart and 70% protamine-crystallised aspart)	5–15 min	1–4 h	24 h				
Basal-bolus regimen	Short-acting human insulin TDS with basal/intermediate-acting human insulin, eg, Humulin S TDS with Insulatard BD Rapid acting analogue TDS, eg, lispro (Humalog), aspart (NovoRapid), glulisine (Apidra) with long-acting analogue, eg, glargine OD	Short-acting human insulin 30 min	2–4 h	6–8 h Duration of basal/intermediate acting human insulin: 12–16 h Rapid-acting analogue insulin 5–15 min	30–90 min 4–6 h Duration of long-acting analogue insulin: varies according to choice of basal insulin (18–42 h)	▶ Calculate total daily insulin dose of 0.3–0.5 units/kg body weight; give 50% as basal and 50% as prandial insulin ▶ If already on basal insulin, add 4–6 units prandial insulin	▶ Adjust the basal insulin doses by 2 unit increments to target FPG of 5.5–6 mmol/L, waiting 3–4 days between adjustments ▶ Adjust the short/rapid-acting insulin with dose titration by 10%	Difficulty in complying with multiple injections a day	▶ Commonly involves multiple injections (at least four to six insulin injections a day) ▶ Useful regimen in individuals with a flexible and/or erratic lifestyle, irregular eating habits or shift workers ▶ Improved glycaemic benefits are best achieved in motivated individuals with regular and optimal insulin dose titration

*Individual patient factors, their experience with hypoglycaemia and higher costs incurred needs to be taken into account prior to the use of newer long-acting analogues.
†Need for diligence when prescribing higher strength insulins.
DPP, dipeptidyl peptidase; FPG, fasting plasma glucose; GLP, glucose-like peptide; OD, once daily; OHA, oral hypoglycaemic agent.

Source: Gururaj SS, et al. Postgraduate medical journal. 2016

alone and can be given two or three times a day for convenience. Premixed insulins carry the same risk of hypoglycemia and weight gain as regular insulin. As basal-bolus treatment is seen as difficult and burdensome, adherence becomes tougher. Medical advancements can simplify treatments, boost convenience and enhance adherence. Insulin pump technology and rapid-acting insulin have enabled CSII to mimic natural insulin release closely. This benefits patients in reaching treatment goals and improving adherence, not just those with T1DM but also intensively managed T2DM. The safety and efficacy of insulin pumps for T2DM were demonstrated in the Opt2mise program. Patients failing to achieve adequate glycemic control with MDI saw significant and lasting improvements in glycemic outcomes after switching to insulin pump therapy.

Healthcare professionals should tailor treatments to each patient's needs, discuss with them their options and educate them on insulin therapy. Basal insulin is preferred as an augmentation therapy when added to oral hypoglycemic agents. If necessary, premixed insulin or a basal-bolus regimen with a correction dosage as part of replacement therapy should be considered. When selecting a therapy, factors like glucose control, side effects, cost, adherence and quality of life should be taken into account. To maintain glycemic control and avoid complications related to diabetes, insulin dosage must be gradually increased. Premixed analog is an excellent alternative with less rigorous glucose monitoring and injection schedules, even though basal-bolus resembles natural insulin secretion. The insulin treatment should be tailored to suit patients, not the other way around.

SENSITIZING T2DM INDIVIDUALS ON INSULIN WITH ORAL DRUGS FOR BETTER GLYCEMIC CONTROL

A growing number of individuals are experiencing significant insulin resistance, leading to the need for substantial insulin dosage. Patients necessitating >1 U/kg/day are categorized as having insulin resistance, while those requiring >2 U/kg/day exhibit severe resistance. The management of individuals with pronounced insulin resistance presents challenges as standard treatment is unable to achieve optimal blood sugar control. Furthermore, concerns such as weight gain, hypoglycemia, treatment complexity and expenses become prominent as insulin doses rise. Consequently, the integration of insulin sensitizers alongside insulin becomes advantageous for these patients as it can address insulin resistance and potentially enhance pancreatic β-cell function preservation or improvement.

1) Metformin

Combining insulin with metformin is a common approach. In various U-500 regular insulin studies, patients typically continued metformin usage. For patients without severe insulin resistance, metformin helps by lowering insulin needs, positively affecting glycemic control and weight. Notably, the HOME study, the most extensive of its kind, involved 390 T2DM patients on basal-bolus insulin. They were randomly assigned to either metformin (850 mg thrice daily) or placebo. Initially, patients had an average daily insulin dose of about 70 units, an HbA1c of 7.8% and a weight of 86 kg. After 16 weeks, the metformin group showed a substantial HbA1c drop of 0.9% compared to 0.3% with the placebo ($P < 0.0001$). Daily insulin requirements decreased by around 10% (7.2 units) from baseline in the metformin group ($P < 0.0001$) accompanied by a slight but significant 0.4 kg weight reduction ($P < 0.0001$).

2) Thiazolidinones

Thiazolidinediones (TZDs) act as "insulin sensitizers," directly addressing insulin resistance mechanisms. These effects not only enhance insulin sensitivity and glycemic control while reducing insulin needs but also potentially benefit other aspects of cardiovascular dysmetabolic syndrome. TZDs are commonly combined with insulin in clinical practice. In a 16-week study, Rubin et al. illustrated that administering pioglitazone at daily doses of 15 mg and 30 mg to patients with a median insulin dose of 60.5 units led to average reductions in fasting plasma glucose (FPG) by 36 mg/dL and 49 mg/dL and reductions in HbA1c by 0.7% and 1.0% respectively, compared to placebo.

CONCLUSION

An ideal first-line strategy is to start insulin with basal insulin and gradually increase the dose to increase the possibility of achieving fasting blood glucose targets. Combination therapy, which combines basal insulin with either an SGLT-2 inhibitor or an incretin-based medication, has complimentary profiles and may be used to treat obesity or a subset of patients who cannot reach glycemic goals even with higher insulin dosages. It may also further offer weight loss with an insulin-sparing effect. The inclusion of post-prandial insulin, a short-acting GLP-1 agonist or a twice-daily biphasic regimen is a helpful solution if post-prandial hyperglycemia is not adequately controlled.

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TIME-IN-RANGE AND OPTIMAL USE OF CONTINUOUS GLUCOSE MONITORING (CGM)

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INTRODUCTION

Self-monitoring of glucose using finger-stick devices, which is now approximately a 50-year-old technology, is promulgated as the principal glucose monitoring method for various reasons. More recently, the introduction of continuous glucose monitoring (CGM) has offered an advanced glucose monitoring technology, both in retrospective and in real-time. The currently available CGM devices measure glucose levels in the interstitial fluid (ISF) through a tiny sensor inserted subcutaneously under the skin, usually on the abdomen or on the arm. The sensor measures glucose levels every few minutes and transmits the information wirelessly to a monitoring device. As these devices got further refined in their features and accuracy, CGM became increasingly reliable and effective in terms of improving HbA1c, reducing hypoglycemic and managing glucose levels in time-in-range (TIR). The major advantage of CGM is that it improves the quality of life of people with diabetes by allowing informed diabetes management decisions.

EVOLUTION OF CGM IN INDIA

CGM illustrates the effectiveness of digital healthcare by utilizing its three components: the medical device, the data-mining engine platform and the data-driven medical feedback. In India, the evolution of CGM started with the availability of Gold CGM system followed by iPro2 (Medtronic). India was the first country to receive approval for the FreeStyle Libre Pro Flash Glucose Monitoring System in 2015. In 2018, Guardian Connect, the first real-time CGM, was launched in India. Following this, in 2020, India saw the launch of FreeStyle® Libre, the intermittently scanned CGM (isCGM).

TYPES OF CGM DEVICES

CGM systems are classified based on their intended use as professional or blinded CGM (P-CGM), intermittently scanned CGM (isCGM) and integrated CGM (iCGM) and real-time CGM.

1) Professional or Blinded CGM

Professional CGM is intended for professional use by healthcare professionals (HCPs) and does not provide the glucose results in real time but downloads the readings after they have been collected. This allows HCPs to obtain relatively unbiased glucose patterns in patients during everyday life. The Endocrine Society recommendations state that professional CGM is especially beneficial to adults with diabetes to detect nocturnal hypoglycemia, dawn phenomenon and post-prandial hyperglycemia, as well as to assist in the management of diabetes. FreeStyle® Libre Pro Flash Glucose Monitoring System is the only available professional CGM in India.

2) Intermittently scanned CGM (isCGM)

isCGM continuously measures interstitial glucose levels and provides glucose data, but requires the user to scan the sensor to obtain information. FreeStyle Libre is an apt example of an isCGM.

Characteristics of intermittently scanned CGM

- The system utilizes two components: a combined glucose sensor with transmitter and a separate touch-screen reader device

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- One hour warm-up period
- Factory calibrated; does not require calibration
- Scanning the reader will provide glucose level, the direction and velocity of changing glucose and an 8-hour trend graph. The patient needs to scan data at least every 8 hours to avoid data gaps
- Does not offer alerts or alarms.

3) Integrated CGM (iCGM)

iCGM can be used as part of an integrated system with other compatible medical devices and electronic interfaces, which may include automated insulin dosing systems, insulin pumps, blood glucose meters or other electronic devices used for diabetes management.

4) Real-Time CGM (rtCGM) or Personal CGM

Real-time CGM automatically transmits both the trend and numerical values of glucose in real-time to a receiver, smart watch or smart phone. For the real-time monitoring of glucose, rtCGM uses sensor electrodes and small filaments inserted into the subcutaneous tissue with an introducer needle. The sensor electrodes measure the glucose level in the interstitial fluid through a glucose oxidase reaction, with the simultaneous generation of an electric signal corresponding to the glucose level. This signal is transmitted continuously *via* radio frequency to the receiver, where the electrochemical signal gets converted into a glucose reading and displayed for the user. The user can set the system to notify them when their blood sugar levels are too high or too low. Some of the globally available rtCGMs include Guardian Connect, Dexcom G5, Dexcom G6, Dexcom G7, Eversense Implantable CGM and Libre 3.

CGM DEVICES IN INDIA

1) Guardian Connect

The Guardian™ Connect continuous glucose monitoring (CGM) system is the standalone CGM system from Medtronic designed for the periodic monitoring of glucose levels in the interstitial fluid under the skin among individuals with diabetes Type 1 and Type 2. The Guardian™ 4 smart CGM system is updated to provide more access and improved performance. In comparison to previous versions, the sophisticated system actively provides variable alert volume, enhances battery life and offers a setup tutorial. It eliminates the need for finger prick and implements user interface changes. Guardian Connect utilizes Guardian Sensor 4, the Guardian Connect transmitter and the Guardian Connect app to transmit data *via* Bluetooth every 5 minutes to the user's smart phone or device *via* the Guardian Connect App *via* CareLink personal and professional software. Guardian Sensor 4 requires two daily finger stick calibrations and is certified for use as an adjunctive device to supplement data collected from regular blood glucose monitoring devices. Its indications are for seven days of continuous usage. The sensor is powered by the Guardian Connect transmitter, which also gathers and processes sensor data. The data is then transferred over Bluetooth to the Guardian Connect app on a smartphone that is compatible with the device. Only patients with a compatible mobile device and enough skill to modify their device's audio and notification settings are supposed to use the Guardian Connect app. The app displays the data, provides a user interface for sensor calibration, enters data such as exercise and meals and uploads information to the CareLink Personal website. The app is also useful for detecting trends and tracking patterns in glucose concentrations.

2) FreeStyle® Libre Pro Flash Glucose Monitoring System

FreeStyle® Libre Pro Flash Glucose Monitoring System was the first professional CGM that does not require finger-prick blood glucose calibration and received FDA approval in 2016 with a featured Mean Absolute Relative Difference (MARD) of

12.3%. The FreeStyle Libre Pro Flash Glucose Monitoring System has three main parts namely a handheld reader, a disposable sensor and FreeStyle Libre Pro software. After the insertion of the sensor by the HCP, the reader component of the system stays with the HCP and the patient can leave the clinic. The sensor can store glucose readings for up to 14 days in 15-minute intervals throughout the day. Patients can produce the sensor for the HCP after the allotted period for analysing glucose reading and can adjust therapy.

3) FreeStyle Libre

FreeStyle Libre is a CGM system consisting of a handheld reader and a disposable sensor worn on the arm as shown in figure 1. Patients four years of age and up are supposed to utilize it as a non-adjunctive treatment. The sensor measures glucose levels continuously for eight hours using a thin, flexible filament that is placed just under the skin. The system has a sensor wear time of 14 days and a warm-up period of one hour. FreeStyle Libre automatically calculates the percentage of time spent above and below the target range and helps to increase the glucose level within the range, which in turn will have a direct impact on the HbA1c reduction.

Figure 1

FreeStyle Libre

Source: Abbott Launches FreeStyle® Libre System in India, 2020

CLINICAL EVIDENCE ON THE POTENTIAL BENEFITS OF CGM

Mounting evidence on the potential benefits of using CGM has popularized the acceptance of CGM devices among a wider spectrum of patients with diabetes. Among the currently available CGM devices, many scientific studies have explored the potentialities of FreeStyle Libre in the optimal management of diabetes. For instance, a study by Haak et al. that assessed the safety and efficacy of new flash glucose-sensing technology to replace self-monitoring of blood glucose (SMBG) revealed that FreeStyle Libre use in Type 2 diabetes with intensive insulin therapy reduces hypoglycemic and offers a safe, effective replacement for SMBG. Another study by Fokkert et al., which was conducted among patients with Type 1 and Type 2 diabetes, demonstrated that the use of FreeStyle Libre flash glucose monitoring (FSL-FGM) had decreased disease burden, improved glycemic control and hence improved the quality of life. In this regard, patients with Type 2 diabetes on LAI and non-insulin (including GLP-1) medication were assessed for changes in HbA1c from baseline to 6 months and baseline

to 12 months following the implementation of a FreeStyle Libre system, in a retrospective observational study by Eugene et al. This suggests that a clinically significant reduction in HbA1c after FreeStyle Libre use supports the real-world effectiveness of the device in patients with Type 2 diabetes using long-acting insulin or non-insulin therapies. A retrospective, blinded evaluation of glycemic control by Kesavadev et al. in 296 T2DM adults for 6 months following a 6- to 7-day study of their glycemic profile using masked P-CGM revealed that it can provide actionable data and motivate patients for diabetic self-care activities, which have enhanced glucose control in comparison to a variety of baseline treatments. Another study by Kesavadev et al., which assessed the clinical utility of FSLP among patients with Type 2 diabetes, showed an improved clinical profile at 6 months as seen from the baseline changes in mean HbA1c, mean FBS, mean PPBS and BMI. All these studies provide ample evidence on the effectiveness of using CGM devices in glycemic management.

THE OTHER CGM DEVICES

1) **Eversense E3 CGM**

   Eversense E3 CGM is an implantable CGM that has been approved by the FDA and lasts for up to 180 days. The health care professional can insert the device letting the users avoid the burdensome self-insertion process every 7–14 days. The sensor requires two calibrations per day for the first 21 days of insertion. Glucose readings and trend arrows provided every 5 minutes help users manage diabetes before going too high or too low on sugars. Eversense can send pop-up messages on the phone and sound an alert or vibrate on the user's arm to alert highs and lows based on customized settings. Eversense uses a gentle silicone-based adhesive that is non-irritative and gentle on the skin. Eversense is yet to be launched in India.

2) **FreeStyle Libre 3**

   FreeStyle Libre 3 is a third-generation CGM system that provides continuous, real-time glucose readings automatically to smart phones for people with diabetes aged 4 years and older. The FreeStyle Libre 3 system includes the long-lasting, smallest, thinnest and most self-applied wearable CGM sensor. The sensor is easy to apply with a one-piece applicator and is worn on the back of the upper arm, eliminating the need for painful finger prick. It features optional alarms, 14-day wear, high accuracy and time-in-range graphs and an ambulatory glucose profile (AGP). It is the "smallest and thinnest" CGM sensor to date, having shrunk by 70% from previous versions. It is approved for usage in Type 1 diabetic pregnant women as well as those with gestational diabetes. This device is not currently available in India.

3) **Dexcom G7**

   Dexcom G7 is the thinnest CGM ever available, approved by the FDA for people with all types of diabetes aged 2 years and older. The device is set up with a combined sensor and transmitter design and once the sensor's run is finished, the user can dispose of the whole combined unit. The G7 is designed to eventually provide a sensor wear time of up to 14 to 15 days. G7 possesses a 30-minute warm-up period before displaying the glucose data.

TIME-IN-RANGE

Time-in-range (TIR) has recently evolved as an important metric to provide meaningful insights into the glycemic control of people with diabetes. TIR is a collective outcome of extensive research by diabetes experts to establish a credible, realistic parameter "beyond HbA1c" to evaluate glycemic management. It can be described as the percentage of time a person's blood sugar level stays within the preferred target range, which is typically 70–180 mg/dL.

The wider acceptance and use of continuous glucose monitoring (CGM) by patients with diabetes globally has demonstrated that the information produced by CGM devices over

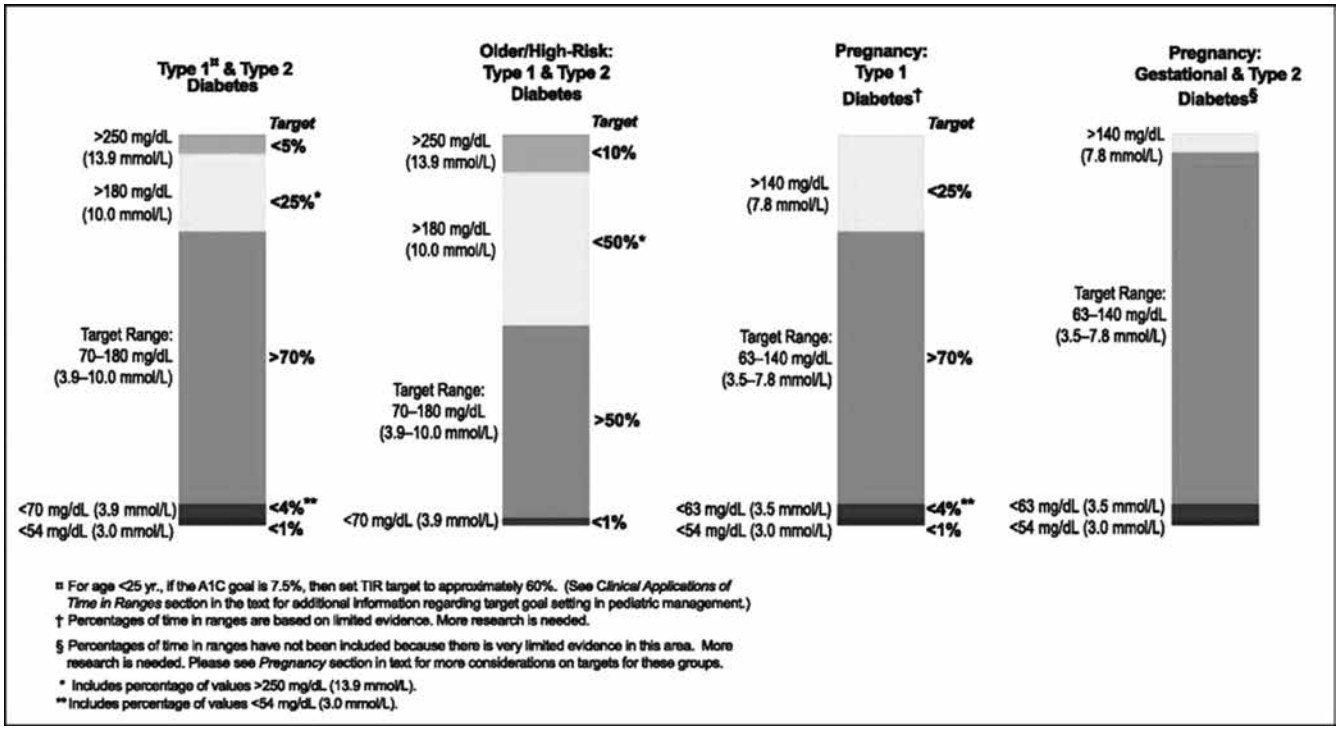
the course of 10 to 14 days provides a more accurate representation of CGM parameters over the course of 3 months. According to the international consensus on time-in-range, TIR should be regarded as the principal CGM-derived parameter defining short-term glycemic management because it provides more valuable information than HbA1c alone. The panel established specific target ranges for identifying different diabetes populations, mainly pregnant women and high-risk groups.

TIME-IN-RANGE GOALS

The IC-TIR (International Consensus on Time-in-Range) expert panel recommends a target range of 70–180 mg/dL for individuals with Type 1 diabetes and Type 2 diabetes and 63–140 mg/dL during pregnancy, along with a set of targets for the time per day [% of CGM readings or minutes/hours] as shown in figure 2. TIR simplifies the crux of these values, such that a patient with diabetes should aim to spend at least 17 hours a day or more than 70% of their time in the blood glucose range of 70–180 mg/dL. This statement also draws a direct relationship between TIR and HbA1c in such a way that every 10% increase in TIR can be considered equivalent to an approximate HbA1c reduction of 0.5% [5.5 mmol/mol] in Type 1 diabetes or 0.8% [8.7 mmol/mol] in Type 2 diabetes. However, the target range was lowered for pregnant women to 63–140 mg/dL as the blood glucose levels are lower during pregnancy. The recommendations also outline fixing targets for people with diabetes who are older and/or considered high-risk and the TIR bar was set at >50% for this category. Scientific evidence on the reliability of this newly introduced metric strongly recommends the inclusion of TIR as a routine parameter for the evaluation of glycemic control and also underlines the possibilities of various complications if TIR is not maintained properly, such as increasing the risk of retinopathy by 64%, nephropathy by 40% and neuropathy by 25%.

Figure 2

Time-in-range targets for different diabetes population



Source: Battelino et al. Diabetes care, 2019

CLINICAL EVIDENCE ON THE BENEFITS OF TIME-IN-RANGE

Several studies have revealed the benefits of TIR as a metric for glycemic control. For instance, a study by Kesavadev et al. evaluated the relationship between TIR and HbA1c in the Asian-Indian population. CGM data from the electronic medical record (EMR) of patients with Type 1 and Type 2 diabetes (n = 424), followed up by telemedicine, were used for the study and analysed using the Mann-Whitney U test, T-test, ANOVA and Pearson correlation. The result showed that TIR should evolve as a powerful target and predictor of diabetes complications and should be a routine measure in diabetes management. Another study by Kesavadev et al. analysed the relationship between time-in-target (TIT) and HbA1c in Asian Indians revealed a close alignment with TIR in accordance with the IC-TIR for HbA1c <7% and between 7-9%. However, in subjects with HbA1c between 9% and 10%, the correlation is weaker or not significant, implying the role of TIR as complementary and not as a replacement for HbA1c. In the elderly, TIR becomes significant as HbA1c drops below 8%. Kesavadev et al., in one of their studies that assessed the clinical utility of TIR in T2D management, revealed that a persuasive case can be made for TIR's strong correlation with both micro- and macrovascular problems and it needs to be regarded as a key performance indicator for the treatment of Type 2 diabetes. A recent study by the same peer group also proposed TIR recommendations for South Asians, which slightly differed from the recommendations by the IC-TIR panel.

CONCLUSION

The use of CGM for diabetes self-management has been proven to dramatically improve the control of blood glucose levels and hence, the quality of life. With abundant information on the percentage of time spent in, above and below the recommended ranges, TIR provides more useful data on the glycemic profile of patients with diabetes. The cutting-edge idea of illustrating TIR with CGM devices leverages immense diabetes management support for patients to achieve the target level and for HCPs to take timely decisions. Considering the multitude of benefits, the use of CGM devices and regularized TIR evaluation should be encouraged both at the patient and at the HCP level.

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PREVENTION STRATEGIES IN TYPE 2 DIABETES: SECONDARY PREVENTION AND REVERSAL

Priyangee Lahiry*

SECONDARY PREVENTION IN TYPE 2 DIABETES

Secondary prevention refers to strategies aimed at mitigating the impact of a disease that has already manifested. In diabetes, this implies the prevention or delay of the complications of diabetes. This can be achieved through early detection, monitoring, meticulous glycemic control and other associated metabolic parameters.

DIABETES SCREENING: A STRATEGY FOR EARLY DETECTION

In India, about 57% of people with diabetes remain undiagnosed or a diagnosis occurs following the detection of a serious complication. Hence, the first step in secondary prevention would be regular screening of asymptomatic individuals for early detection. The importance of early detection in reducing long-term complications has been documented in many studies. Silico analysis of data from the ADDITION-Europe study revealed a higher reduction in absolute and relative risk for CV outcome at 5 years with early screening and detection when compared to 3 or 6 years of delay.

All adults, 30 years of age and older, should be screened annually and more often if initial screening reveals prediabetes. Recently, it has been suggested that screening for diabetes in India should be initiated at the age of 25 for non-pregnant adults, particularly overweight and obese individuals with a family history of diabetes. Similarly, children and adolescents with a family history of diabetes or with risk factors like polycystic ovarian syndrome (PCOS) should be screened starting at 10 years of age or since the onset of puberty, whichever comes first. Screening and addressing modifiable risk factors for CVD including dyslipidemia, hypertension, smoking and alcohol consumption should be conducted simultaneously.

A two-step detection approach involving the identification of high-risk individuals with the help of a risk assessment questionnaire, followed by glycemic measurement in these high-risk individuals should be adopted and screening should be made opportunistic rather than community-based to make it more targeted and cost-effective.

MONITORING AND MANAGEMENT OF DIABETES: IMPORTANT STRATEGIES FOR SECONDARY PREVENTION

The key to minimizing the impact of diabetes and preventing or delaying its complications is good metabolic control right from the beginning. This involves not only glycemic control but also control of lipid parameters, blood pressure and body weight. This can be achieved through regular monitoring of the following:

- Fasting plasma glucose (FPG) and post-prandial glucose (PPG) lab tests are done once a month and more often if values are not in the target range
- HbA1c every 6 months and every 3 months if targets are not met
- Clinical examination at every visit
- Routine examination of the foot at every visit and foot care education
- Monitoring weight, waist circumference and B.P.
- Self-monitoring of blood glucose (SMBG)

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Annual monitoring to be done of the following test:

- Blood urea, serum creatinine
- Blood lipids
- Urine protein/albumin
- Retinal checkup (fundus examination for retinopathy)
- Detailed foot examination: palpitation of the dorsalis pedis, posterior tibial pulses, monofilament and vibration perception testing (VPT)

DIABETES MANAGEMENT STRATEGIES

The main modalities of Type 2 diabetes mellitus (T2DM) management include:

- Pharmacotherapy
- Lifestyle Modification
- Behavioural Medicine

Pharmacotherapy

While lifestyle modifications remain the cornerstone of interventions, in overt T2DM, pharmacotherapy is an indispensable component of management and secondary prevention. Pharmacological agents in the management of T2DM include not only the use of oral antidiabetics, insulin and other injectables but also preventive pharmacotherapy for primary cardio-vascular prevention. While treatment algorithms provide a standardized framework for physicians to make evidence-based decisions considering patient characteristics and disease progression, it is important to tailor interventions to each patient's unique needs to optimize glycemic control while minimizing the risk of complications.

Importance of managing post-prandial hyperglycemia and glycemic variability

The conventional approach to diabetes management has typically revolved around reducing HbA1c levels with a focus on controlling FPG. However, it is currently recognized that solely addressing fasting hyperglycemia does not lead to optimal glycemic control. As individuals approach their target HbA1c levels, the relative impact of post-prandial glucose becomes more pronounced compared to fasting glucose levels. Apart from this, post-prandial hyperglycemia is an independent predictor of cardiovascular risk and mortality as well as all-cause mortality. A significant increase in carotid intima thickness has been observed with increased post-prandial (PP) glucose levels. PP-hyperglycemia is also associated with microvascular complications and it has been observed that a reduction in PP glucose leads to reduced incidences of nephropathy and retinopathy. Reducing PP-hyperglycemia can reduce with endothelial dysfunction, thrombosis, inflammation and oxidative stress.

Glycemic variability (GV) refers to the fluctuations in glycemic parameters over a given interval of time. Both short-term (day-to-day or intra-day fluctuations*)* and long-term (variation in HbA1c and FPG between visits) GV is associated with macro- and microvascular complications, hypoglycemia, an increased mortality rate and adverse clinical outcomes.

Thus, in the secondary prevention of T2DM, the management of PP-hyperglycemia and the prevention of GV are of utmost importance in addition to maintaining HbA1c targets. These aspects should be monitored regularly and managed accordingly. Pharmacological agents that target post-prandial glycemia include GLP-1 receptor agonists, GIP-based medications, DPP-4 inhibitors, prandial insulins and alpha-glucosidase inhibitors. Along with medications, targeted dietary strategies and exercise can be used to address post-prandial glycemia as well as GV.

Lifestyle Modification

The following aspects of lifestyle modification should be addressed as basic strategies for secondary prevention in T2DM which mainly overs medical nutrition therapy and structured exercise plan.

Medical Nutrition Therapy (MNT)

An individualized lifestyle modification with dietitian-guided MNT and a structured exercise plan has been shown to have better outcomes compared to general diabetes education and support.

The basic guidelines for MNT in T2DM are summarized in Table 1. The carbohydrate and protein recommendations shown in the table are based on recent suggestions made by Anjana et al. 2022, based on the ICMR-INDIAB National Study.

Post-prandial glycemia is more prominent in Asians due to the carbohydrate content of meals. Management of PP-hyperglycemia is crucial for long-term glycemic control and the prevention of cardiovascular complications in T2DM. Thus, specific dietary strategies aimed at managing post-prandial hyperglycemia should be incorporated into diet planning and counselling. Some of these strategies include nutrient preloading, food sequencing, modifying macronutrient composition and dividing large meals into smaller portions.

Table 1
Summary of basic guidelines for MNT in T2DM

Energy	CHO*	Protein*	Fat	Fibre	Micronutrients	Na+
	49-54%	**19-20%**	**25-30%**	**25-40g**	**RDA, 2020**	**1500-2300mg**
Calorie Reduction of 500-750 Kcals/day	• Low GI, unrefined cereals, whole fruits, legumes • Simple sugars, refined carbs, processed cereals to be avoided	• High B.V sources • Lean meat, fish, egg white, soya, legumes and pulses	• MUFA-10-15% • PUFA-8-10% (n6:n3-5-10:1) • SFA <10%; <7% with elevated lipids • Transfat: Nil • Oil Rotation	Soluble Fibre-15g	• Adequate K+ intake • Mg, Ca, Zn, Cr, Se, Thiamine • Routine supplementation not recommended • B12 monitoring & supplementation in Metformin users	• Added salt <5g; <3g for HTN • Packaged and canned foods to be avoided
* Shashank R. Joshi, et.al., 2022 Macronutrient Recommendations for Remission and Prevention of Diabetes in Asian Indians Based on a Data-Driven Optimization Model: The ICMR-INDIAB National Study						

Reproduced from Source: Anjana RM et al., The ICMR-INDIAB National Study. 2022.

Structured Exercise Plan

It is important to individualize exercise regimens based on psychological, cardiovascular and musculoskeletal status. In general, 150 minutes of moderate-intensity (50–70% max heart rate) aerobic physical activity per week divided between 3 days per week with no gap of more than 2 consecutive days without exercise should be aimed. Pre-prandial resistance training and post-prandial (post-breakfast) moderate exercise have been demonstrated as good strategies to reduce post-meal glucose excursions and improve insulin resistance. Training of the inspiratory muscles, short-term interval walking and frequent interruptions of prolonged sitting with 3 minutes of light-intensity walking breaks every 15 minutes have been shown to reduce glycemic variability in T2DM patients.

Behavioural Medicine

Apart from medications, diet and lifestyle modifications, the role of behavioural medicine intervention is of utmost importance. The prevention and management of any disease boils down to a behavioural issue. Even the best of recommendations will not work unless

patients comply with the advice given. Educating patients about the consequences of poor control, understanding the barriers to compliance and motivating them to modify their behaviours that will positively impact their health and diabetes outcome is very important.

REVERSAL OF DIABETES

The concept of diabetes reversal is evolving continuously, driven by advancements in our understanding of the underlying pathogenic mechanisms and natural history of T2DM. A paradigm shift has occurred, challenging the traditional belief that T2DM is an inevitably progressive and incurable condition necessitating ongoing medication adjustments.

Return to normoglycemia can occur either spontaneously or following specific interventions in some people with T2DM and might persist after the withdrawal of glucose-lowering agents. However, it is to be noted that this return to normoglycemia might not be permanent and thus the accepted terminology in this regard is "remission".

Background

Following bariatric surgery, insulin secretion normalizes and glucose levels return to normal levels. This can be maintained for long term without medications if the weight loss is maintained. The sharp decrease in calorie intake after the surgery is the reason for the return to normoglycemia, which occurs in response to the fall in liver fat level, improvement in hepatic insulin sensitivity and consequent normalization of FPG. This observation led to the postulation of the twin cycle hypothesis of the etiology of T2DM. Chronic positive energy balance, in the presence of pre-existing muscle insulin resistance, leads to excess liver fat deposition. This in turn causes hepatic tissues to become resistant to insulin's suppression of hepatic glucose output. To compensate for this excess glucose in the blood, basal insulin secretion is increased, which perpetuates the vicious cycle of hyperinsulinemia and hepatic insulin resistance. In order to get rid of the excess hepatic fat, hepatic VLDL export is increased and if the subcutaneous fat depot is unable to accommodate this fat, ectopic fat buildup occurs in other organs like the pancreas. In people with susceptible beta cells, this can cause beta cell dysfunction, leading to disruption in the mealtime insulin response and an increase in post-prandial glucose levels. These self-reinforcing cycles lead to the onset of T2DM. Thus, it was postulated that if the root cause, that is, excess calorie intake can be addressed, this sequence of events can be reversed. This formed the basis of the concept of the reversal of diabetes.

Definition and Criteria for Remission

Being able to maintain HbA1c levels below a certain threshold without any anti-diabetic therapy is regarded as a remission of diabetes. The criteria of remission have evolved over the last decade, with previous consensus categorizing remission into "partial" and "complete" using different glycemic thresholds. However, in reality, fluctuations in blood glucose can happen even in people in T2DM remission and it was realized that this categorization could bring about problems in diagnostic coding and affect insurance policy decisions, hence it was rejected and the criteria have been simplified.

According to the latest global consensus which was formulated by the American Diabetes Association (ADA), the Endocrine Society and the European Association for the Study of Diabetes (EASD) in 2021, the criteria for remission are as follows:

- HbA1c <6.5% or FPG <126 mg/dL (or estimated HbA1c <6.5% calculated from CGM values); maintained without anti-diabetes drugs for at least 3 months.
- Three months and not earlier after stopping glucose-lowering medications, testing of the HbA1c level should be done to confirm a remission.

Calorie Restriction, Weight Loss and Remission of T2DM

It has been widely demonstrated that weight loss achieved through caloric restriction can improve insulin sensitivity, glycemic parameters and contribute to a decreased medication prescription.

In the UKPDS study, normalization of glucose levels in 15% of the participants was observed following the initial dietary weight loss phase. In the Look AHEAD trial, 11.5% of the participants receiving intensive lifestyle intervention achieved partial or complete remission.

The twin cycle hypothesis was tested in the counterpoint study, in which normalization of insulin response and restoration of beta cell function were demonstrated with the use of a very low-energy liquid dietary regimen for 8 weeks in overweight and obese subjects with a duration of diabetes within 4 years. This was the first human trial to show that beta-cell dysfunction can be corrected with sustained caloric restriction.

However, the major landmark trial in this area was the DiRECT trial, running across 49 primary care centres in Scotland, in which an intervention with a very low-calorie liquid dietary regimen for 3-5 months and structured support for long-term weight maintenance in healthy T2DM subjects led to remission in nearly 50% of the subjects with a mean weight loss of 15 kg. This was followed up in a larger cohort and also replicated in other populations and similar results were obtained.

Determinants of Remission

Although it has been demonstrated that remission of diabetes is possible, it cannot be achieved by everybody. Age, degree of weight loss, maintenance of lost weight, duration of diabetes, mental health status and ability to adhere to strict diet and lifestyle measures are some of the important determinants of remission.

Positive outcomes have been observed in younger patients with good mental health status and most importantly, in subjects with a shorter duration of diabetes, i.e., within 6 years of onset and ideally 2 years. Also, the amount of weight loss that is required is much greater than what is conventionally advised.

It is known that, with time, there is a loss in functional beta cell mass in people with T2DM. This happens due to glucotoxicity from chronic hyperglycemia as well as lipotoxicity, which causes beta cells to de-differentiate, leading to a loss of their secretory capacity. As discussed, sustained negative energy balance can eliminate excess pancreatic fat, but whether that will lead to remission of diabetes depends on the amount of residual beta cell mass with functional reserve. It appears that beyond a certain point, beta cell function cannot be restored. Thus, in patients on multiple antidiabetic agents, the chances of remission are poor since irreversible beta cell damage would have already taken place in these cases.

Factors to Consider

While the reversal of diabetes is an appealing concept and is marketed as an alternative to conventional diabetes management, a few points should be kept in mind. Firstly, remission is not a permanent state and does not mean diabetes is cured. Stringent lifestyle and dietary control have to be maintained, failing which, hyperglycemia will recur. Also, the chances of complications cannot be ruled out even when remission is achieved because the harmful effects of prior hyperglycemia might persist in various tissues as "metabolic memory." Hence, periodic monitoring of HbA1c (at least annually) and monitoring of weight, blood pressure, lipids, renal function and retinal screening should be continued. Lastly and most importantly, as discussed earlier, not every patient with diabetes can achieve remission. Remission can be considered in patients who are obese, young, with new onset or a shorter duration of diabetes and most importantly, in people who are motivated enough to adopt and adhere to stringent lifestyle and dietary measures. Patients with long-standing diabetes who are on multiple antidiabetic agents, patients with poor glycemic control, patients with diabetic complications and pregnant individuals should be discouraged from attempting to achieve remission.

SUMMARY

While the concept of diabetes reversal is appealing, the primary focus in T2DM should be on secondary prevention, which emphasizes

long-term disease management. Remission may be achievable for some, but in general, focusing on long-term disease management can help minimize the risk of complications and prevent morbidity and premature mortality.

A more sensible approach to addressing T2DM should include a balanced combination of medications, dietary adjustments and exercise rather than pursuing medication-free remission through unrealistic dietary measures alone. By adopting this approach, individuals can achieve manageable and sustainable control of their condition, promoting overall well-being and better quality of life.

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QUESTION AND ANSWERS

Q: Why use Time-in-Range? Is it accurate?

A: The period of time spent in the target blood glucose (blood sugar) range typically between 70 and 180 mg/dl, is known as "time in range" (TIR). Processing this data from your continuous glucose monitoring (CGM), it reflects how long the blood glucose has been within the target range and how often one has hyperglycemia or hypoglycemia. TIR reflects an ideal glycemic control since it helps lower the risk of microvascular complications such as retinopathy, peripheral neuropathy and microalbuminuria.

Different types of DM are likely to be optimally controlled in different TIR. The T1DM and T2DM population will fall approximately 70% of the time in the TIR of 70-180 mg/dL, whereas an elder person with T2DM falls only 50% in the same TIR of 70-180 mg/dL. But they led to reflect values which fall almost 60% in the TIR of 180-250 mg/dL. Similarly, Type 2 diabetes with pregnancy show 90% of readings in the TIR of 63-140mg/dL. On the other hand, a Type 1 pregnancy show >70% readings in a TIR of 63-140mg/dL. This displays the finer nuances of optimal glycemic control required in different populations. The TIR for each group varies. Hence in practice the target glycemic range for every group is to be individualised. This makes TIR a flexible range with a different target range for different groups of people with diabetes.

Q: With what frequency should you use CGM?

A: Daily and weekly summaries are useful for monitoring glycemic control. CGM can be used to evaluate daily excursions of blood glucose and interpret these results along with the food-activity pattern to get meaningful results. It is used frequently if the individual with diabetes mellitus repeated history of hypo-hyperglycemia, poor control and a highly variable lifestyle. It can be used once in 3 months to match the pattern with HbA1c outcome.

Q: What are the considerations when attempting remission of Type 2 diabetes?

A: We should identify which candidate is suitable for remission of T2DM. A non-pregnant adult who has previously had T2DM for a shorter duration, suffers from excess body weight is an ideal candidate. An individual suffering from atherosclerotic cardiovascular disease (ASCVD), heart failure (HF), chronic kidney disease (CKD) and under 60 years of age with no cardiovascular risk factors and not on any cardiorenal protective drugs, would not be recommended for remission.

Q: How do you manage blood sugar and ketone levels in blood while using an insulin pump?

A: Managing blood sugar and ketone levels while using an insulin pump is crucial. It is usually seen in TIDM. Ketone levels increase rapidly due to any interruption of insulin supply from the insulin pump because there is no insulin available for more than 10-15 minutes. Check the blood sugar and ketones if interruption in basal insulin delivery lasts longer than an hour.

Causes of ketone build-up:

- Missed insulin dose due to air trapped in the tubing.
- Extended pump disconnections or suspensions exceeding two hours.
- Issues with the pump such as insulin leakage (at the point of insertion or connection between the infusion set) or spoiled insulin.
- Factors such as infection, dehydration and vomiting.

Hence, the caregiver should screen for symptoms

indicating a potential diabetic ketoacidosis (DKA) state observed as unexplained blood sugar spikes, continuous high levels, vomiting and/ or nausea.

Treatment: One can be treated using "KISS" mnemonic**.**

K: Examine for Ketones; I: Inject Insulin (with a syringe or insulin pen; do not use a pump); S: Modify the infusion set; S: Verify your blood sugar

Sick-Day Routine: If one develops diarrhoea, vomiting or fever and is unable to eat or retain normal meals, one needs to follow a sick-day routine. Purpose is suspended if there is moderately severe intercurrent illness.

- Take daily dose of insulin even if unable to eat.
- Test urine/blood glucose every 4 hours, especially if urine glucose is 1mg% or more or blood glucose exceeds 200 mg%.
- Administer additional short-acting insulin if ketones accompany high glucose levels. Refrain from using additional insulin if only ketones are present without elevated urine glucose (less than 1mg%).

Managing Illness:

- Have someone to take care of you.
- Stay hydrated, rest and keep warm. Use water, fruit juices, regular soft drinks, tea and broth. After improvement, switch over to soft and later to solid diet.
- If unable to tolerate solid food, consume liquids every hour.
- Adjust insulin dosage as per physician's guidance.
- Avoid exercise.

*Extra Insulin Administration***:**

- Administer 20% of regular daily insulin dose every 3-4 hours if needed.
- Example: If usual daily dose is 40 units, take 8 units every 3-4 hours depending on outcome of blood and urine tests.
- If symptoms persist, contact diabetologist or go to hospital emergency.

Seeking Medical Help:

- Contact physician if vomiting, in pain or symptoms persist despite management.
- Report to emergency room if symptoms worsen or unrelieved.

Adhering to these guidelines would assist individuals on insulin pump to effectively manage their blood sugar and ketone levels while minimizing the risk of DKA complications.

JJ

RECIPES

VEGETABLE AND TOFU SOUP

INGREDIENTS

- 100 gm extra-firm Tofu, drained and cut into 3/4-inch cubes
- 50 gm diced Tomatoes
- 50 gm fresh Carrot
- 50 gm green Beans
- 50 gm chopped Bell pepper
- 1 tsp Oregano
- 1 tsp crushed Black pepper
- 1 tsp Garlic
- 1 tsp Lemon Juice
- 1 tsp Salt
- 1 tsp Olive oil
- Few Coriander leaves
- 250 ml Vegetable Broth

METHOD OF COOKING:

1) In a pot with heated oil, sauté freshly chopped coriander. Sauté coriander rapidly to preserve its flavour and aroma.
2) Include all the vegetables and sauté it on high flame for a minute.
3) Next, add the diced tofu and cook it evenly.
4) Add the seasonings and vegetable broth. Subsequently, let it simmer for a few minutes to ensure thorough blending of all components.
5) Finally, take it off the stove and squeeze in the lemon juice.

Provides 2 servings

Nutritional information per serving

Energy (Kcal)	Carbohydrate (gm)	Protein (gm)	Fat (gm)
100	10	7	3

Special Features:

- A healthy soup
- A recipe rich in protein and low in fat

SHAHI TOFU

INGREDIENTS:

- 200 gm block of firm Tofu
- 100 gm Tomatoes, chopped
- 50 gm low-fat Yogurt
- 1 tsp cooking Oil
- 1 tsp Ginger, minced
- 2 green Chillies, chopped
- 2 green Cardamom, crushed
- 50 gm red Onion, sliced
- 4 no. Cashew
- ½ tsp red Chili powder
- ½ tsp Garam masala
- ¼ tsp ground Turmeric
- 1 tsp Kasoori Methi
- Salt to taste

METHOD OF COOKING:

1) Give tofu a 15-minute press. After the tofu is pressed, cut it into rectangles that are ½ inch thick and combine it with some salt and red chili powder.
2) Fill the pan with 1 tsp oil and heat it to medium. Next, add the ground cardamom (from two green cardamoms), ginger and green chilies. Before adding the onions, stir for one minute. Stirring often, cook for 5 minutes or until onion is transparent.
3) Include tomatoes and cashews. Turn up the heat to medium-high and shut it off. On medium-high, cook for 7–8 minutes. At least once throughout this time, uncover to stir.
4) Add the yogurt and simmer for five minutes over medium heat, uncovered. Take the pan off of the burner. Blend its ingredients after letting it cool slightly. If more water is needed for blending add ¼ cup.
5) Pan-fry the tofu in a small amount of oil while the gravy cools. Fry for 3–4 minutes on each side or until browned but not very crisp.
6) In another skillet, heat up another 1 tsp of oil over medium-low heat and sauté the red chili powder, Kashmiri lal, garam masala, turmeric and kasoori methi for around a minute or until aromatic.
7) Transfer the gravy to the skillet. To clean the remaining parts of the blender, use ¼ cup of water. If needed, add a bit more water and salt.

Provides 4 servings

Nutritional information per serving

Energy (Kcal)	Carbohydrate (gm)	Protein (gm)	Fat (gm)
90	5	7	5

Special Features:

- A healthy recipe
- A recipe rich in protein and low in fat

HOW KNOWLEDGEABLE ARE YOU?

1) Glycogenolysis is metabolic conversion of:
   A. glycogen into glucose
   B. glucagon into glucose
   C. glucose into glycogen
   D. glucose into glucagon

2) Which of the following is the scientific name for Splenda?
   A. Sucrose
   B. Sucralose
   C. Saccharin
   D. Sorbitol

3) According to the ADA, people with Type 2 diabetes should be screened for microalbuminuria/ GFR:
   A. five years after diagnosis and then yearly
   B. at diagnosis and then yearly
   C. the onset of renal failure and then yearly
   D. with the first signs of hypertension and then yearly

4) ABC in diabetes denotes
   A. A-HbA1c, B-Blood Pressure, C-LDL-Cholesterol
   B. A-Ankle Brachial Index, B-blood urea, C-Cholesterol
   C. A-HbA1c, B-Bilirubin, C-Creatinine

5) Olive oil and canola oil are rich sources of:
   A. Monounsaturated fat
   B. Polyunsaturated fat
   C. Saturated fat
   D. Trans fat

6) The average blood glucose increases by approximately _____ mg/dL for every 1% of HbA1c.
   A. 20
   B. 35
   C. 40
   D. 25

7) Which of the following is a true statement about diabetes and alcohol?
   A. People with diabetes should not drink alcohol
   B. Alcohol stimulates glycogenolysis
   C. Hypoglycemic can occur 8-12 hours after drinking alcohol
   D. Alcohol is a source of glucose

8) When evaluating the effectiveness of a carbohydrate-to-insulin ratio, it is important to consider:
   A. Intake of carbohydrate
   B. Timing of exercise
   C. Post-prandial blood glucose levels
   D. All of the above

9) If you are sick how often should you check your blood sugar levels?
   A. Once a day
   B. 10 times in a day
   C. Every 2 – 4 hours
   D. Not required to check

10) The leading cause of death for people with diabetes is:
   A. Amputation
   B. Kidney failure
   C. Pancreatic neoplasm
   D. Heart disease

ANSWERS:

1. A	2. B	3. B
4. A	5. A	6. B
7. C	8. A	9. C
10. D		

MYTHS AND FACTS

Myth: The insertion of CGMS is painful

Fact: CGM offers a gentle and non-invasive approach to monitoring glucose levels. The thin sensor inserted under the skin typically causes minimal discomfort. Unlike needle or syringe injections, CGM tests interstitial fluid just beneath the skin, not blood. Occasionally, individuals may experience skin irritation due to the adhesive used to secure the device in place. Research on CGMS, including measurements of adherence, demonstrates that they are generally well-accepted.

Myth: No more fingerprick needed and once the CGM is initiated

Fact: While CGM's significantly reduces the number of fingerprick required, there are certain times when they are needed to verify levels. Unlike SMBG, a CGM sensor actually takes readings from one's interstitial fluid and not directly from the blood. Because the readings are from two different places, there is a natural lag between glucose levels in the interstitial fluid and glucose levels in the blood. Therefore, it is normal and should be expected, for the sensor readings and BGM readings to be different but for the most part they should be close.

Myth: Sensor cannot get wet and cannot be read through clothing

Fact: It is completely fine to shower and bathe and go for normal daily activities while wearing a CGM. The sensor is water-resistant and can also be worn while swimming and exercising. It is recommended that "the sensor not be submerged in water deeper than 1 meter or kept underwater for longer than 30 minutes at a time. The reader, however, is not waterproof and should be kept nearby and out of the water." Results can also be read through clothing, including winter sweaters and jackets Additionally, the reader can collect data within a range of 1 to 4 cm from the sensor.

Myth: Insulin always needs to be refrigerated

Fact: Insulin does not always need to be refrigerated. Many people store open bottles and cartridges at room temperature because they find it more comfortable to inject. Opened and unopened insulin can be stored at room temperature for up to 28 to 30 days, hence extra insulin supply must be refrigerated. Refrigerated, unopened bottles are good until the expiration date printed on them. Always read the instructions that come with your insulin.

JJ

CERTIFIED DIABETES EDUCATOR COURSE

Dr Chandalia's DENMARC in association with Help Defeat Diabetes Trust (HDDT) presents to you a course to be a Certified Diabetes Educator (CDE)!

Help Defeat Diabetes Trust (HDDT) is a registered, non-profit public trust, having amongst its many objectives, the main objective of promoting education and awareness about diabetes among people from different fields.

Who can enroll?

Graduates in Nutrition, Doctors, Nursing, Pharmacy, Occupational and Physiotherapy.

What is the duration of the course?

6 months, including 3 months (300 Hours) of hands-on training and experience with a recognized mentor in your own town (see this on our website).

How can I do this course from my place of residence?

A Suitable Mentor can be selected from the registrant locality under whom the training can be done.

How will I get the course material?

All course material is available online on our website.

What are the course fees?

The standard fee for the course are INR 10,000/- only.

Where can I get more information about this course?

Kindly visit our website **http://www.helpdefeatdiabetes.org** or you can get in touch with us on our email id: heldefeatdiabetesinfo@gmail.com.

MEMBERSHIP FORM

Association of Diabetes Educators (ADE)

(For eligibility criteria: Check Website www.diabeteseducatorsindia.com)

Name …… Date of Birth: ……

Address ……

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Telephone: Res: …… Office: …… Cell: ……

E-mail id: ……

Educational Qualifications:……

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Work Experience: ……

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Currently employed at: ……

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Certificates attached*: ……

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Please pay the membership fees through NEFT / RTGS to the following bank account.

Account name: Association of Diabetes Educators
Account type: Savings Account
Name of the bank: Bank of India
Account number: 006610110001734
IFSC Code: BKID0000066

……
Signature

CHALLENGES IN DIABETES EDUCATION

AN AWARD FOR PROBLEM RESOLUTION IN DIABETES EDUCATION

SPONSORED BY DR. CHANDALIA'S HELP DEFEAT DIABETES TRUST

Prize money of Rs. 10,000 for reporting a problem case

Dr. Chandalia's HDDT aims to enhance the quality of Diabetes education in India by creating a world-class research and education environment and to build up a platform of networking and knowledge sharing within diabetologists and/or diabetes educators.

Challenges in Diabetes Education 2023 places special emphasis on supporting educational initiatives that have the potential to improve and significantly revolutionize diabetes care, enhance self-management and/or support patients with Type 1 or Type 2 Diabetes Mellitus. The educator should describe an individual or group case history and identify the problem in diabetes education. Furthermore, s/he should describe the plan of education to resolve the issue, partly or totally. The issue described may be related to patient perceptions, knowledge, behaviors and implementation of advice given. S/He should describe her struggle in resolving the issue including her triumphs and failures, the methodologies used and ethical, socio-economic and behavioral aspects of the case.

General Rules and Regulations regarding the eligibility Criteria for the Award

- The applicant of the Award should be a citizen of India and member of Association of Diabetes Educators.
- The case discussion should be on the subject of Diabetes Education.

The best case chosen by a group of referees will be awarded "Challenges in Diabetes Education Award- 2023" which will carry a cash prize of Rs 10,000. The awardee will get the opportunity to present the case in the annual meeting of Association of Diabetes Educators and publish it in the journal of Diabetes Education.

The last date for the submission is 30th December, 2023 !!!!

(Instructions for authors is available on website www.diabeteseducatorsindia.com)