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To Dispel Darkness of Diabetes

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CONTENTS

INTERACTION OF INDIAN CULTURE AND MODERN MEDICINE

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I have completed 50 years of practice of Endocrinology and Diabetes in India on my return from USA in January, 1971. It has been a great experience, as each patient I saw was a different human being having his/her own ideas of the disease s/he was suffering from, its causation and its treatment.

Over the course of five decades my thought processes about the state of my interaction with my patients kept churning and in the past one decade I came to an important conclusion: that my patients in India were vastly different from those I saw in the USA for a 4-year period. I expect that people in different countries will differ, but as I went deeper into this subject, the differences got magnified.

This article is based upon an analysis of these socioeconomic and cultural factors that prevail in our country. They have a high impact on the quality of medical care delivered and accepted by our people. Their most significant impact is on the continuity of care and treatment adherence.

POOR KNOWLEDGE OF HEALTH ISSUES AND ALTERNATE HEALTHCARE SYSTEMS

Our population, even if educated, is not very knowledgeable on health-related issues. The science behind health issues is not taught during our basic education. It is imbibed slowly by those who are educated in general and additionally have an open mind: which we know is a hall-mark of scientific temperament.

Our education system has supported the theory that each student should learn 3 languages. Their mother tongue, regional language if different from the mother tongue and language being used as a medium of instruction if it is different from the above two languages.

Although for all practical purposes 3 languages can be learnt by any student, the depth of learning is affected, most specifically in the area of health sciences. Hence the communications between the Healthcare Professional (HCP) and patients are poor.

In all counties in the world some degree of fake information and pseudoscience is propagated. I have found this being practiced in the health farms of Switzerland, where many myths are perpetrated regarding the efficacy of their specialized, expensive and exotic treatments. The truth and science is wrapped in a mystical make-believe package in a very sophisticated manner which raises the narrative to a level that patient is not able to decodify the ethical from unethical treatment. In India, such a culture is also rampant and the outcome of the same is faced by us day to day. Besides the home remedies and folklore, which surprisingly may have a scientific basis at times, the alternate systems of medicine perpetuate concepts that are not amenable to analysis through any standard scientific method. In fact, it is propounded by the proponents of Alternate systems that the established modern science is incapable of understanding these issues as the basis of each disparate system is unique and claimed to be unfit for analysis under any other conceptual framework. Aayush is a conglomerate of a group of incongruous medical systems, each of them having its origin in different parts of world and each is based upon different theory and principles. That being so, putting them together in a single group is a mistake even if it is being done as a matter of convenience.

Ayurveda is a system of medicine having its origin in India from the Vedic period. It finds

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its mention in Atharv Veda and to some extent in Rigveda. It is extensively used in India for more than 3,000 years ago and has texts and treatises written by masters. The approval of an Ayurvedic remedy is currently done by regulatory authorities based on these texts. To my mind the validity of any therapeutic approach or product should be explored by the current method of scientific inquiry. Although the mechanism of action of Ayurvedic remedies have their own explanations, their efficiency and adverse effects are amenable to modern methods of clinical studies. As an example, this has been done extensively in case of Ayurvedic remedies for the treatment of Type 2 diabetes. The leaves, root and bark of more than 200 plants is known to possess glucose lowering capacity. Many of them have been studied as per modern methods and data is published in current scientific journals. As Editor of the International Journal of Diabetes in Developing Countries, four such peer-reviewed studies were evaluated by me and published in the years 2007 to 2009 (Table 1). These articles showed efficacy of these herbal products. In fact, I along with my colleagues in the Research Society for the Study of Diabetes in India (RSSDI) launched a study on the role of Yoga and debittered Fenugreek powder in the prevention of Type 2 diabetes. It is indeed necessary and desirable to subject such products to modern scientific scrutiny and adopt them for use in niche areas of therapeutics. However, such an approach is not yet introduced for all these products by the regulatory bodies, so that these medications continue to be used, shrouded in the myths and mysteries of old Ayurvedic texts.

Patients in India have an implicit faith in Ayurvedic medications. This is a cultural phenomenon, as highly educated patients also demonstrate this faith. Out of a large number of Type 2 diabetics treated at our center, majority had been on the Ayurvedic drugs or home remedies. Even if their blood glucose was high, they believed that the Ayurvedic medication was producing some beneficial effect. When prescribed effective modern drugs, they were keen on continuing Ayurvedic drugs. It was with great difficulty that we could dissuade them from this practice. When simultaneous use of both systems is continued, we have to contend with the fact that any side effect is likely to be attributed to modern medicine and any good effect attributed to Ayurvedic drugs. We need to develop a complete line of argument to curb such practices by the patients. If patients are very keen on using Ayurvedic drugs, you are likely to counter this firmly. However, such an approach will be considered unfair by the patient. Hence, practioners of modern medicine have to develop well-informed and open-minded approach to convince the patient about the undesirability of following such practices. I try to achieve this by saying: “I agree with you that there are more than 200 plants whose roots, leaves or bark have a mild glucose lowering effect. This can be used to treat Type 2 diabetic patients during the early course of their disease. In fact modern science should find the rightful place for these remedies and the most logical situation is to use these products in impaired Glucose Tolerance Group or for the prevention of Type 2 DM. However, in a Type 2 diabetic of 10 year duration having a HbA1c of > 8%, these drugs will fail to produce any effect”. Such open-minded approach will inspire our patient’s confidence in us. Scientifically, it will be a valid approach.

ATTITUDE, BEHAVIOR AND ADHERENCE

All HCP’s interact with a large number of patients with diabetes. They are applying their mind closely to the history, physical examination and test data presented by their patients. Simultaneously patient’s attitude and behavior registers imperceptibly in their minds and impacts their responses.

In India and may be in many other countries there is a hugh trust deficit between the doctor and patients. The causes of this trust deficit needs in-depth study. In general, people in India have a low level of trust with each other. It arises from centuries of unreliable and untruthful behavior by a large segment of population, thus fostering the trust-deficit in each sphere of our activities. The same fact holds true of many other Asian countries. Our culture has immense difficulty in separating a truth from a lie. The reason being we have a range of truths, for example “absolute

Table 1:
Studies Published in the Journal of International Journal of Diabetes in Developing Countries

Article	Year	Author
Effect of *Trigonella foenum-graecum* seeds on the glycemic index of food: A clinical evaluation	2007	Preethi B. Gopalpura, C. Jayanthi, Sonal Dubey
Evaluation of the phytochemicals and antidiabetic activity of *Ficus bengalensis*	2007	Sharad Sharma, Mamta Chaturvedi, E. Edwin, Shruti Shukla, Hemant Sagrawat
Lipid abnormalities in streptozotocin-diabetes: Amelioration by *Morus indica L.* cv Suguna leaves	2009	B. Andallu, A. V. Vinay Kumar, and N. Ch. Varadacharyulu
Study of glucose uptake activity of *Helicteres isora Linn*. fruits in L-6 cell lines	2009	R. N. Gupta, Anil Pareek, Manish Suthar, Garvendra S. Rathore, Pawan K. Basniwal and Deepti Jain

truth" and "apriya truth" (Harsh Truth, Truth that offends). Our mythological heroes were allowed an occasional lie, although they were otherwise epitomes of ethical and moral standards. When we develop our thought processes on this background we find difficult to trust others. Very rarely, we will trust a guru or mentor, but that is also doubtful. The Doctor Patient relationship has suffered from the same malady. Add to this a few glaring examples and practices which are occasionally detected in the conduct of a HCP. The trust-deficit is not a recent phenomen, it is an old one. A shloka reflects this poignantly.

वैद्यराज नमस्तुभ्यं यमराजसहोदर । यमस्तु हरति प्राणान् वैद्यो प्राणान् धनानि च ? हे वैद्यराज, यम के भाई, मैं आपको प्रणाम करता हूँ. यम तो सिर्फ प्राण हर लेते है पर आप धन और प्राण दोनों हर लेते हो !!

O vaidya (doctor), brother of Yama(God of Death), I bow down to you. Yama only steals away one's life, but the vaidya steals one's life as well as money.

Fortunately, Trust-Deficit is not universal, hence, most of the time we are able to establish a meaningful doctor patient relationship, albeit with great difficulty.

We believe in absolute integrity of our body; it should not be invaded by doctors who may mount an assault on us by their thought-processes and therapeutics and ruin our peace of mind. Furthermore, medications and injectables are considered unholy invasions of body. There is a constant endeavor to get rid of this invasion; hence we keep trying to reduce the pills, injections and investigations prescribed by doctors. Poor adherence to medications is common world over; but the cause of this in the Western world usually is forgetfulness. In India, the foremost cause could be willful negligence. Most of my diabetics ask me if their disease can be reversed or their medications can be reduced or stopped. They repeat this question at each visit. Of course, a small proportion of recently discovered Type 2 diabetes can be reversed by a good life style intervention. But overall the disease is not curable or permanently reversible. Hypothyroidism is so simple to treat; one needs to master only the dose adjustment with thyroxin. However, very ingeniously one of my patients told me that he was very unhappy because of his poor prospects of gaining freedom from this daily dose of medication. I told him this is a natural product, in fact exactly what the body makes; hence he should accept it wholeheartedly. I explained that at time reversal is possible, depending upon the cause and severity of the disease. The next question was: Doctor, if I cannot be cured, will it possible to do a transplant of the thyroid gland? He had to be educated upon the fact that suppression of immunity by an immunosuppressant carries great dangers for him compared to a daily intake of a thyroxin tablet.

CONTINUITY OF CARE

This is very important in dealing with chronic disease like diabetes, hypothyroidism, chronic obstructive lung disease, rheumatoid arthritis and similar diseases. It calls for considerable discipline and motivation on the part of the patient. Human being do not want to be dictated by other as freedom is dear to all humans. Similar rebellious trend of thoughts pervades our mind. Regimentation is repugnant to must of us. From these statements, a small degree of non-adherence to the scheduled follow up visits is expected. However, a gap of a few years in place of a quarterly visit needed for a Type 2 diabetic is a frequent phenomenon in our patients which needs further analysis.

What could be the cause of this behavior? One important cause is that patients pay from their pockets for the ambulatory care as the insurance companies hardly cover any such costs. The bills are quite high when modern drugs are used. This needs correction by the health care policy planners. We must at least cover economically weaker sections of our communities. But those affording the healthcare costs need education on the benefits of continuous care of a chronic disease. Another reason for the poor continuity of health care is poor organization of health care services. Patients are not given the follow up appointment neither are they reminded to attend the clinic on a scheduled appointment date and time. Even in advanced countries, where such systems are set up, the between-visit intervals are not planned on the basis of medical needs, the reason being non-availability of the HCP's in required numbers. Currently, the health-care administration has started questioning of such practices. Inertia in treatment of diabetes has been highlighted in many research papers. Logically, if the effect of a treatment modality is fully manifest in 2 weeks, there is no reason why an appointment is scheduled after 2 months. Some of these issues can be partly resolved by involving paramedical personnel in diabetes centers. This explains our efforts to develop a well-trained cadre of diabetes educators.

CONTINUOUS GLUCOSE MONITORING AND TIME-IN-RANGE*

Gopika Krishnan, Sreelakshmi R, Anjana Basanth

INTRODUCTION

Continuous glucose monitoring (CGM) is an advanced blood glucose (BG) monitoring technology, both in retrospective and in real-time. Currently available CGMs measure glucose level 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 level every few minutes and transmits the information wirelessly to a monitoring device. The accuracy of CGM is generally assessed using the metric, Mean Absolute Relative Difference (MARD). Implementation of CGM as a vital element in diabetes management which aids both patients and health care professionals (HCPs) in improving the quality of life (QoL) and in taking timely decisions respectively. Intensive research to integrate CGM with automatically controlled insulin delivery has progressed incrementally towards a fully functional artificial pancreas/Automated Insulin Delivery System (AID).

HISTORY OF CONTINUOUS GLUCOSE MONITORING

Self-monitoring of glucose using finger-stick devices, which is now a 50-year-old technology, paved new paths for individuals afflicted with diabetes to have better control of the disease. This has culminated at present into Continuous Glucose Monitoring devices. As these devices got further refined in their technical features and accuracy, CGM becomes increasingly reliable. CGM has demonstrated efficacy in terms of improving HbA1c, reducing hypoglycemia and improving the time in target. CGMS Gold introduced by MiniMed Medtronic which was approved for marketing by the Food and Drug Administration (FDA) in 1999 was the predecessor of the current CGM systems. Further developments in CGM systems facilitated the introduction of more advanced systems such as the iPro2 with Enlite sensor. The first "real-time" CGM was the Glucowatch Biographer. Currently available CGM systems in India include FreeStyle Libre Pro, Guardian Connect and FreeStyle Libre.

CONTINUOUS GLUCOSE MONITORING IN INDIA

CGM consists of three components: the medical device, the data-mining engine platform, and the data-driven medical feedback. In India, the evolution of CGM had started with the availability of CGMS Gold, iPro2 (Medtronic). This blinded CGM, was the most popular CGM for about a decade. Further, India was the first country to receive approval for FreeStyle Libre Pro Flash Glucose Monitoring System in 2015. In 2020, FreeStyle® Libre, the intermittently scanned CGM (isCGM)), was launched in India. Despite the Covid pandemic, it was widely accepted by the physicians and patients. Obviously, the provision of real-time glucose values, patterns, Time-in-Range (TIR) and the platforms to download, store and share data inspired patients with diabetes to adopt CGM devices.

CLASSIFICATION OF CGM SYSTEMS

CGM systems are classified based on their intended use as Professional/ Blinded CGM (P-CGM), Real-time CGM, intermittently scanned CGM (isCGM) and Integrated CGM (iCGM).

PROFESSIONAL/ BLINDED CGM

Professional CGM is intended for professional use by HCPs to personalize therapy adjustments

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that may reduce glucose variability and improve HbA1c in patients with diabetes. It does not necessarily 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 of 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 postprandial hyperglycemia and also to assist in the management of diabetes therapies.

iPro2

Medtronic's iPro2 P-CGM received FDA approval in 2016. iPro2 collects and stores data from a glucose sensor which can be uploaded into CareLink iPro® Therapy Management Software for Diabetes (CareLink iPro, MMT-7340), to generate reports. The system can collect up to seven 24-hour periods of data. The device stores data up to 144 h (6 days). The reported overall Mean Absolute Relative Difference (MARD) of iPro2 is 13.6% .Table 1 describes the features of the currently available Professional CGMs.

Table 1:

Features of the currently available Professional CGMs

System Type	Device	Wear time duration of sensor	Calibration required	Frequency of glucose readings	MARD	Data accession Software/devices
Professional CGM	iPro2	6-7 days	No	Every 5 minutes	13.6%	Data can be downloaded using CareLink™ iPro software & can be uploaded from sensor recorder using CareLink iPro website.
	Libre Pro	14 days	No	Every 15 minutes	12.3%	Data scanned from sensor using FreeStyle Libre Pro reader in provider's office

Source : Chamberlain JJ.;2018

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 BG calibration and received FDA approval in 2016 with a featured MARD of 12.3%. FreeStyle Libre Pro Flash Glucose Monitoring System has three main parts: a handheld reader, a disposable sensor and FreeStyle Libre Pro software as shown in figure1. After the insertion of the sensor by 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 at 15-min intervals throughout the day. Patients can bring the sensor to the HCP after the allotted period for analyzing glucose readings and adjust their therapies.

Figure 1:

FreeStyle Libre Pro

Source: Blevins TC, 2010

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. The characteristics, advantages and disadvantages of isCGM are described in Table 2 and Table 3 respectively.

Table 2:

Characteristics of isCGM

Characteristics of isCGM
System utilizes two components: a combined glucose sensor/transmitter and a separate touch screen reader device.
1 h warm-up period
Factory calibrated; does not require calibration
Scanning the reader will provide glucose level, the direction & velocity of changing glucose and an 8 h trend graph. The patient needs to scan data at least every 8 h to avoid data gaps
Does not offer alerts/alarms

Source: De Ridder, et al; 2019

Table 3:

Advantages and disadvantages of isCGM

Advantages of is CGM	Disadvantages of isCGM
Adjunctive use	User needs to scan the sensor to get the reading
Calibration is not required	Sensor needs to be scanned at least every 8 h to capture full 24 h data
Longer sensor-wear life (14 days)	No alarms/alerts for impending hypoglycemia or hyperglycemia events
Blood ketone tests with special test strips	
Can be used in pregnancy	
Glucose measurement- 40-500 mg/dL	
Lower cost than RT-CGM	

Source: Ziegler R, et al, 2021

FreeStyle Libre

Freestyle Libre is available in India for adults and children (above the age of four) and women with gestational diabetes. The FreeStyle Libre sensor measures glucose every minute in interstitial fluid through a small filament inserted just under the skin and held in place with a small adhesive pad. A quick scan of the sensor with a reader provides a real-time glucose reading on-demand and a complete picture of a person's glucose levels, without painful finger pricks as shown in Figure 2.

Figure 2:

FreeStyle Libre

Source: https://www.medicaldevice-network.com/projects/freestyle-libre/, 2014

Real-Time CGM (RT-CGM) or Personal CGM

RT-CGM is one among the recent technological innovations in diabetes care that can automatically transmit 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, RT-CGM 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 (IF) through a glucose oxidase reaction with 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 displays it for the user. The system can be programmed to alert the user when glucose levels are too high or too low. The advantages and disadvantages of RT-CGMs are described in Table 4. Some of the globally available RT-CGMs include Guardian

Connect, Dexcom G5, Dexcom G6, Dexcom G7, Eversense Implantable CGM and Libre 3.

GUARDIAN CONNECT

Guardian Connect utilizes Guardian Sensor 3, Guardian Connect transmitter, and Guardian Connect app to transmit data *via* Bluetooth every 5 minutes to the user's smart phone or device as shown in Figure 3. It is indicated for the periodic monitoring of glucose levels in the IF under the skin, in patients with 14 to 75 years of age. Guardian Sensor 3 is indicated for 7 days of continuous use and is approved for use as an adjunctive device to complement information obtained from standard blood glucose monitoring devices and requires 2 daily finger stick calibrations. It is a stand-alone system which displays glucose data for the previous 3, 6, 12 or 24 hours. The system possesses personalized alerts and alarm features, including adjustable volume settings throughout the day and at night, and snooze feature, to silence CGM alerts for a period of time. The Guardian Connect app is intended for use only by patients using a compatible mobile device, and who have sufficient experience in adjusting mobile device audio and notification settings. The app displays data, provides a user interface for sensor calibration, data entry on exercise and meals and upload information to the CareLink Personal website.

Figure 3:

Guardian Connect ™

Source: https://www.medtronicdiabetes.com/products/guardian-connect-continuous-glucose-monitoring-system, 2024

EVERSENSE E3 CGM

Eversense E3 is the world's first long-term CGM which has been approved by the FDA for people with diabetes aged 18 years and older with exceptional accuracy and a fully implantable sensor that lasts for up to 180 days. HCPs can insert the sensor, 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 wear. Glucose readings and trend arrows help users to manage diabetes before going too high or too low. Eversense can send pop-up messages to phone and sound an alert or vibrate on user's arm to alert highs and lows, based on customized settings. Eversense is yet to be launched in India.

FREESTYLE LIBRE 3

FreeStyle Libre 3 is a third generation CGM system which provides continuous, real-time glucose readings automatically to smart phones for people with diabetes aged 4 years and older. FreeStyle Libre 3 includes long-lasting, smallest, thinnest and 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 sticks. The system includes FreeStyle Libre 3 mobile app, which enable users to capture and view their real-time glucose levels, glucose history and trend arrows showing changes in glucose in their smartphone. The device has been clinically proven to improve glucose control, increase time in target glucose range, decrease time in hyperglycemia, hypoglycemia and lower HbA1c. It features optional alarms, 14-day wear, high accuracy and time- in- range graphs and ambulatory glucose profile (AGP). This device is not currently available in India.

DEXCOM G6

Dexcom G6 is the first CGM system approved by the FDA in March 2018, to use as an 'integrated' CGM alongside other diabetes management devices such as insulin pumps, closed-loop systems and BG meters. G6 system is suitable for determining BG levels in children aged two or older and adults with diabetes. It features a 10-day sensor and requires zero finger pricks or scanning. Real-time glucose readings are sent to user's smart devices or receivers every 5 minutes. In terms of accuracy, Dexcom G6 features an overall MARD of 9.0%. Its use is

clinically proven to lower HbA1c, reduce hyper- and hypoglycemia, and increase TIR. Use of the Dexcom CLARITY software can facilitate better decision-making by analyzing a patient's glucose data during telehealth or in-person visits. This device is not currently available in India.

Dexcom G7

Dexcom G7 is the thinnest CGM ever available. The **fully disposable** device is set up with a combined sensor and transmitter design. Once the sensor's run is finished, the user can dispose the whole combined unit. G7 is designed to eventually provide a sensor wear time for up to 14 to 15 days. It has a 30-minute warm-up period before displaying the glucose data. The accuracy of Dexcom G7 using MARD is calculated as 8.1% in children and 8.2% in adults. Dexcom filed the G7 with the FDA by the end of 2021 and the approval is expected in 2022.

Table 4:
Advantages and Disadvantages of RT-CGMs

Advantages	Disadvantages
RT-CGMs provide real-time feedback to patients allowing them to observe the effects of food, activity, stress, alcohol, and other factors on their blood glucose levels.	Frequent alarms could make patients feel that they are failing to reach their target blood glucose levels and can lead to increased anxiety.
Greater Improvement in the quality of life in patients as compared to SMBG.	Alarm fatigue describes situations in which patients receive so many CGM alarms that they become less likely to respond appropriately leading to less-than-optimal use of RT-CGM and discontinue the CGM use.
Data collected on CGM devices can be uploaded to a computer for graphing and further analysis using software and apps.	Patients who use CGM systems express concern about having a device connected to their body, which increases their self-consciousness about diabetes and also reveal that they have diabetes.
Provide insights into glucose trends that allow patients to act preemptively to avoid hyperglycemia or hypoglycemia.	Some RT-CGMs still need finger stick calibrations and confirmation of hypo or hyperglycemia before taking necessary actions.
Trend arrows feature in context to current glucose levels increase patients increase their confidence in dosing decisions particularly for patients who fear incidences of hypoglycemia or hyperglycemia.	The lag time is reported by various CGM devices because of the blood glucose reading taken from IF and does not reflect actual BG concentration that is found in standard finger stick blood samples drawn from capillary blood.

Source: Sun MT, et, 2021

Time-in-range

Time-in-range is defined as the percentage of time an individual spends with their blood glucose levels in the target range. It includes three key CGM measurements: time spent within target glucose range, time spent below target glucose range (TBR), and time spent above target glucose range (TAR) in duration of 24 hrs. For instance, if a person's TIR is 50%, it can be explained as of the 24 hrs duration of a day, the person spent 12 hours within the target glycemic range. The target range varies depending upon the individual, but general guidelines suggest the range as 70 to 180 mg/dL. TIR can be measured accurately by using a CGM device. These devices are equipped with software/apps that automatically record the TIR that helps both patients and health care professionals to derive a clearer picture of their glycemic profile on a timely basis.

Time-in-range Goals

The IC-TIR (International Consensus on Time-in-Range) expert panel recommends a target range of 70-180 mg/dL [3.9-10.0 mmol/L] for individuals with Type 1 diabetes and Type 2 diabetes and 63-140 mg/dL [3.5-7.8 mmol/L] during pregnancy, along with a set of targets

for the time per day [% of CGM readings or minutes/hrs]. 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. However, the target range was lowered for pregnant women to 63-140 mg/dL as the ambient blood glucose levels are lower in pregnancy. The recommendations also outlines fixing targets for people with diabetes who are older and/or considered high-risk and the time-in-range bar was set at 50% for these category. If TIR is not maintained properly it may increase the risk of retinopathy by 64%, nephropathy by 40% and neuropathy by 25%.

Several studies had revealed the benefits of TIR as a metric for glycemic control. For instance, a study by Kesavadev et al., evaluated the relationship between TIR with HbA1c in the Asian-Indian population. CGM data from electronic medical record (EMR) of patients with Type 1 and Type 2 diabetes (n=424) followed up by a telemedicine were used for the study and analyzed using 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 care. Another study by Kesavadev et al., that analyzed the relationship between Time-in-Target (TIT) and HbA1c in Asia Indians revealed a close alignment with TIR in accordance with the International Consensus on TIR for HbA1c <7 and between 7-9% . However, in subjects with HbA1c between 9-10% the correlation is weaker or not significant implying the role of TIR as complementary and not as a replacement for HbA1c. In elderly, TIR becomes significant as HbA1c drops below 8% . Kesavadev et al., also in one of their studies that assessed the clinical utility of TIR in Type 2 diabetes management revealed that a persuasive case can be made for TIR's has a robust association with micro- and macrovascular complications and should be positioned as an endpoint and valued metric for Type 2 diabetes management. A recent study by the same group also had proposed TIR recommendations for South Asians which slightly differ from the recommendations by the IC-TIR panel.

CONCLUSION

Time-in-range provides more meaningful data on the glycemic profile of patients with diabetes with ample information on the percentage of time spent in, above and below the acceptable glucose ranges. The wide acceptance of CGM systems globally emphasizes its efficiency in diabetes management. Extensive research and the introduction of innovative concepts in CGM will strengthen the confidence of patients in adapting and using advanced CGM devices for better diabetes management.

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TOBACCO CESSATION STRATEGIES

Jayshri Jain*

Cigarette smoking is a major cause of disease and the leading preventable cause of death. Exposure to second-hand smoke also increases a person's risk of disease and death. Smoking is also associated with many other non-fatal diseases and problems, including osteoporosis, skin wrinkling, peptic ulcer disease, impotence, and pregnancy complications. Even smoking a small amount, such as one cigarette a day, is associated with increased health risks. Researches published in journals bear out a 50% mortality rate in smokers who do not suspend smoking till the age of 35 as compared to a non-smoker. U.S. Department of Health and Human Services, state 74% of smoking evidence in adolescence.

Ingredient inducing dependence on tobacco is nicotine, a substance found in all types of tobacco products. It is imperative to know that nicotine alone is not the only explanation of all the ill effects of smoking. When people refrain using tobacco containing products, majority of them encounter withdrawal symptoms like depressed mood, disrupted sleep, irritability, frustration, anger, anxiety, difficulty concentrating, restlessness, decreased heart rate, and increased appetite or weight gain. This unlikeable temperament drags them back to nicotine.

Tobacco dependence treatment includes singly or in combination, behavioral and pharmaceutical interventions such as brief advice and counseling, intensive support and administration of pharmaceuticals that contribute to reducing or overcoming tobacco dependence in individuals. (WHO evidence-based recommendations on the treatment of tobacco dependence) Nicotine is a speedy matter which acts within 7 seconds of inhalation, stimulating the adrenal glands which release epinephrine which gives a kick to the smoker.

The sprint of adrenaline leads a sudden release of glucose, an rise in blood pressure, and respiratory and heart rates and hyperglycemia.

Extended usage of tobacco products (cigarettes, cigars, pipes, or smokeless tobacco) have revealed increased prevalence of stomach cancer. Dickerson TJ et al proclaims the hazardous effect of Nornicotine (a nicotine metabolite) which causes increased production of advanced glycation end-products (AGE) that are responsible for complications of diabetes, cancer and Alzheimer's disease.

Literature proposes the use of medications along with counseling to assist patients to get relieved from the effect of tobacco. Counseling using different techniques like individual and group analysis and proactive telephone calls have shown its potential advantages for cessation of smoking.

Therapy should involve problem solving techniques like number of cigarettes, number of times and finding a way out when the urge occurs will help patient to abandon smoking.

US FDA has endorsed the use of 5 type of medications to enable the smokers to quit. Of these 4 are nicotine-replacement therapies (gum, inhaler, nasal spray and patch). They relieve nicotine withdrawal symptoms and help to quit smoking by gradually providing the body with smaller doses of nicotine over time, without exposing you to the toxic chemicals found in cigarette smoke. Non-nicotine agent recommended is bupropion which act on pathways in the brain that are involved in nicotine addiction.

1. NICOTINE GUM:

Nicotine gum (Nicotine Polacrilex, Nicorette) generates a rise and fall in the nicotine level

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throughout the day and helps by blocking the urge to smoke. It is imperative to know the way the gum has to be used for its maximum benefit. The gum should be chewed until a peppery taste or tingling sensation occurs and then to place the gum between the gum and cheek to facilitate nicotine absorption through the oral mucosa. This needs to be repeated for 30 minutes.

The recommended dosage for the gum is 2 mg of the gum per day for people who smoke less than 25 cigarettes per day and 4 mg per day for people who smoke more than 25 cigarettes. It is advisable that the smokers utilize this gum on a fixed schedule throughout the day (every one or two hours) so as to avoid alterations in the mood due to declining nicotine level. Eating or drinking is not permissible 15 minutes prior to consuming the gum. The side effect of the gum is sore throat, hiccups, dysgeusia (abnormal taste sensation), dyspepsia, nausea, flatulence and gastrointestinal discomfort. This approach of the use of nicotine gum however is pertinent for a short term withdrawal.

2. NICOTINE PATCH:

A nicotine patch works differently from nicotine gum .These patches are worn for 16 to 24 hours. Literature states that nicotine levels generally rise and form a plateau when the nicotine patch is applied to the skin, wherein it supplies nicotine continuously to the blood stream. Nicotine patch is known to be more beneficial over nicotine gum due to easy use and greater quantity of nicotine supplied to the blood stream. The dosage is decided using Fagerström scale. The recommended dose for nicotine patch are 21 to 22 mg (24-hour patch) and 15 mg (16-hour patch) respectively. Light smokers are begun on a standard dose of 21-22 mg/24 hours. After 4 to 6 weeks the dose is tapered to an intermediate level, 14 mg/24-hour. Following an additional 2 to 4 weeks, the lowest dose of 7 mg/24 hour is used to complete the taper. High dose nicotine patch therapy aids in complete relief from nicotine as well as the withdrawal symptoms. Studies reveal that a 24 hour nicotine patch aids in controlling the morning smoking urges. The harmful effects of the patch include skin irritation, burning, head ache, nausea, vertigo, dyspepsia.

3. NICOTINE NASAL SPRAY:

Nicotine nasal spray mimic nicotine bolus in cigarette and is identified to deliver nicotine level more swiftly than nicotine gum or nicotine patch. The nasal spray brings about a rise in the plasma nicotine levels within 10 minutes. The spray is spurted against lower nasal mucosa. It should not to be sniffed, swallowed, or inhaled. One spray of 0.5 mg into each nostril equals one dose of 1 mg. Patients may use 1 or 2 doses per hour, not to exceed 5 doses per hour or 40 doses per day. An average smoker uses 15 doses per day, decreasing the dosage over time. Smokers use 1 to 2 puffs per hour for 3 months. Adverse effects of nicotine nasal spray include headache, local burning, rhinitis, watering eyes, nasal or throat irritation, sneezing and coughing.

4. NICOTINE INHALER:

The nicotine inhaler is the most referred substitute sensory simulator of cigarettes. The device does not deliver nicotine to the lungs. Once the inhaler is swallowed, its absorption occurs from the oral and pharyngeal mucosa and gastrointestinal tract. If one smoke regularly, it is best to use at least 6 cartridges a day for the first 3 to 6 weeks and can use up to 16 cartridges per day. The adverse effect of the inhaler is throat irritation and coughing.

NON-NICOTINE AGENTS

There are various non-nicotine agents like bupropion, nortriptyline that alter noradrenergic neurotransmission and aid in smoking cessation.

BUPROPION HYDROCHLORIDE

Bupropion is an amino-ketone antidepressant that weakly inhibits both noradrenergic and dopaminergic uptake. The drug works on dopaminergic activity affecting the mesolimbic system and nucleus accumbens, which is the pleasure reinforcing area of the brain for addictive drugs. It also affects the noradrenergic activity in the locus caeruleus, which activates

higher cortical functions such as alertness, concentration and memory. Lack of nor-epinephrine stimulation with nicotine withdrawal may account for withdrawal symptoms. Bupropion may lead to a drop in weight with termination of smoking.

Clinical trials show that bupropion is most effective in combination therapy. Jorenby DE et al have shown burpropion in combination with nicotine patch have shown superior cessation rates as compared to a monotherapy.

Smokers should start taking bupropion a week prior to quitting. Set a date for quitting and stop smoking sometime in the second week of taking the drug. The recommended dosage is 150 mg once daily for 3 days and subsequently 150 mg twice daily for 7 to 12 weeks. It is imperative that there is 8 hour interval between two doses. It is suggested that the dose is taken in late afternoon or early evening so as to avoid insomnia.

Studies propose combined therapy of bupropion and nicotine patches, or nicotine patch and gum. This produces higher quit rates for smokers determined to quit. Apart from medications it is essential to reason out added risk factors for smoking. (e.g., alcohol abuse and depression)

The National Health and Nutrition Examination Survey III (NHANES III) initiated that chewing alternatives can deal with the issues of oral gratification placing a pinch between gum and cheek.

Nogler et al have pointed out beneficial effects of sunflower seeds, bubble gum, sugarless candy, mint in reducing cravings and withdrawal symptoms. Douglas E.J Orenby et all have proven through their work that use of nicotine replacement therapy along with antidepressant like bupropion have shown to help smoking cessation.

An interventional method which involves telephone help-lines are used as counselling wherein the smokers can simply telephone and the counsellor rings back to give ongoing support which can be effective treatment for smokers.

A helpful strategy initiated by the government for tobacco control programs is conducting health campaigns, workplace cessation policies and treatment and smoke-free public places. Professionals play a very important role in supporting the smokers with quitting and mitigating withdrawal symptoms along with the initial support and motivation coming from the family members and dear ones.

These approaches are not alternatives but complementary methods to motivate smokers to quit smoking.

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QUESTION AND ANSWERS

Q. How do you assess iron status of diabetic patient with renal failure?

Ans. Anemia is an early complication of chronic kidney disease (CKD) and causes increased morbidity and mortality. Anemia develops in intermediate stages of CKD and worsens with progression of CKD. The cause of anemia is varied and includes nutritional deficiency, increased pro-inflammatory cytokines, chronic blood loss, and relative erythropoietin (EPO) deficiency. This decrease in EPO matches the decline in kidney function and is the main determinant of anemia in CKD stage 4-5.This rationale forms the basis for treating CKD with erythropoiesis stimulating agents (ESA).

Iron deficiency is common in India because of poor socio-economic status. In addition, CKD is a major cause of morbidity and co-morbidity in India. Considering the combined effects of both the clinical entities, it becomes very important to establish the relation and effect of each of them on the other. The common causes of iron deficiency in this group of patients are usually a combination of poor nutrition, poor intestinal absorption of dietary iron, chronic inflammation, and chronic blood loss. It is also postulated that iron deficiency and low iron stores are the main causes of hypo-responsiveness to ESA therapy. Thus, the use of iron in combination with ESA is usually required for optimal management of the anemia of CKD.

The effective management of anemia in patients with CKD (especially ESRD) requires close monitoring of iron status and adequate replenishment of iron stores especially during treatment with recombinant erythropoietin (rEPO). Because the effectiveness of rEPO therapy is often dependent on the availability of iron, accurate assessment of the iron status of the patient is crucial. Incorrect assessment of iron status may result in inappropriate management of patients, leading to iron deficiency or overload that can cause unwanted oxidative injury.Hence, the assessment of parameters that accurately reflect iron status is important in this situation.

Q. What are the gastro-intestinal side effects of Oral Semaglutide?

Ans. Nausea, vomiting, abdominal pain, loss of appetite, diarrhea, or constipation may occur. Nausea usually lessens as semaglutide is continued.

This medication should be taken with a sip of plain water as directed by your doctor, usually once daily. Do not take it with any other beverage. Swallow the tablet whole. Do not split, chew or crush the tablet. Wait at least 30 minutes after taking semaglutide before you eat or drink anything other than plain water and before taking any other medication by mouth.

For the best effect, you should eat 30 to 60 minutes after taking semaglutide. It is important to maintain the same routine with every dose of semaglutide.

JJ

RECIPES

BANANA COCONUT MILK SMOOTHIE

INGREDIENTS:

100 gm banana slices

100 ml coconut milk

50 gm low fat curd

Ice cubes (optional)

1 tsp Chia seeds (for topping)

PROCEDURE:

1. Take ripe bananas and finely slice it.
2. Take good quality coconut milk.
3. Whisk the thick fresh low fat curd well before putting it into the mixture with rest of the ingredients
4. Blend in all of these ingredients into a mixture until it forms achieves a fine thick consistency.
5. Top it with some extra Chia seeds and serve chilled.

Provides 2 servings

Nutritional information per serving:

Energy (kcal)	Carbohydrate (gm)	Protein (gm)	Fats (gms)	Potassium (Mg)	Glycemic Index
170	16	2.4	11	498	Medium

Special features:

- A healthy recipe for snacks options
- A recipe rich in potassium

AVOCADO, BROCCOLI & BELL PEPPER SALAD

Ingredients

100 gm Avocado cubes

100 gm blanched broccoli florets

100 gm bell peppers (red, yellow)

50 gm tomato cubes

50gm cucumber cubes

50 gm iceberg lettuce (shred into large pieces)

1 tsp roasted flaxseeds (optional)

To mix into dressing:

2 tsp olive oil or cooking oil

1 tsp dried mixed herbs

4 tsp lemon juice

Salt and freshly ground black pepper to taste

PROCEDURE:

1. Prepare the salad dressing first with the help of 2 tsp of olive oil or cooking oil, dried mixed herbs, lemon juice and freshly ground black pepper. Addition of vinegar is optional.
2. Chop avocado, bell peppers, tomatoes and cucumbers into cube sizes
3. Blanch and boil the broccoli very well and chop it finely or keep it the usual size
4. Wash the iceberg lettuce finely in water and then shred it into large pieces.
5. Mix all the ingredients in a big bowl and serve.

Provides 2 servings

Nutritional information per serving:

Energy (kcal)	Carbohydrate (gm)	Protein (gm)	Fat (gm)	Magnesium (Mg)	Glycemic Index
163	8	4.5	13	21	Medium

Special Features:

- A healthy recipe as a mid-morning snack
- A recipe rich in fiber and magnesium

JJ

HOW KNOWLEDGEABLE ARE YOU?

1. Which of the following is not a part of the 'Deadly Quartet' in metabolic syndrome?
   A. Proteinuria
   B. Obesity
   C. Diabetes
   D. Hypertension

2. What is the NCEP/ATP III cutoff for waist circumference in diagnosis of Metabolic Syndrome in males?
   A. >/= 85
   B. >/= 102
   C. >/= 100
   D. >/= 90

3. Which of the following is not a metabolic effect of Insulin?
   A. Promotes glucose entry into cell
   B. Muscle protein breakdown
   C. Fat synthesis in cells
   D. Glycogen deposition in liver

4. Of the following, which is advisable for a well-controlled diabetic?
   A. Exercising on a full stomach
   B. A small carbohydrate (30gms) snack before exercising
   C. Exercising on an empty stomach
   D. Eating a hearty meal immediately after exercise

5. Exchange lists are:
   A. Group of food that contain one food from each of the six food categories
   B. Nutrition lists
   C. Group of food those are interchangeable with each other because of similar carbohydrate, protein and fat content
   D. Diabetic recipe list that are exchanged between people with diabetes

6. The only sulfonylurea permitted to be used in renal failure:
   A. Gliclazide
   B. Glibenclamide
   C. Tolbutamide
   D. Glipizide

7. Drug that has shown positive effect on lipid profile:
   A. Glibenclamide
   B. Glimepiride
   C. Metformin
   D. Vidagliptin

8. Which is the most common side effect of insulin therapy?
   A. Lipohypertrophy
   B. Lipoatrophy
   C. Hypoglycemia
   D. Infection

9. The following food is a potent source of antioxidant:
   A. Rice
   B. Butter
   C. Ghee
   D. Fruits and Vegetables

10. Cholesterol is required by the body to:
    A. Make certain vitamins
    B. Make hormones
    C. Make cell wall structures
    D. All of the above

ANSWERS:

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

MYTHS AND FACTS

1. **Myth: You should avoid all fats if you are trying to be healthy or lose weight.**

   Fact: You do not have to avoid all fats if you are trying to improve your health or lose weight. Fat provides essential nutrients and should be an important part of a healthy eating plan. But because fats have more calories per gram than protein or carbohydrates, or "carbs," you need to limit fats to avoid extra calories. If you are trying to lose weight, consider eating small amounts of food with healthy fats, such as olives and nuts. You also could replace whole-fat cheese or milk with lower-fat versions. Take tips from a diabetes educator about the food portions to consume and how much of food is enough for your body.

2. **Myth: Dairy products are fattening and unhealthy.**

   Fact: Dairy products are an important food group because they have protein which one's body needs to build muscles and help organs work well and also contains calcium to strengthen bones. Most dairy products, such as milk and some yogurts have added vitamin D to help your body use calcium.

   Adults should have 3 servings a day of fat-free or low-fat dairy products, including milk or milk products such as low-fat yogurt and cheese as part of a healthy eating plan. If you cannot digest the lactose sugar found in dairy products, choose lactose-free dairy products or fermented dairy foods and beverages such as yogurt and buttermilk. Include calcium and vitamin D rich food source.

   - Calcium: soy-based beverages or tofu made with calcium sulfate, canned salmon, or dark leafy greens such as collards or kale
   - Vitamin D: cereals or soy-based beverages

3. **Myth: Physical activity only helps if one can do it for prolonged period.**

   Fact: One does not need to be active for long periods to get the amount of regular physical activity requirement which is at least 150 minutes of moderate-intensity physical activity each week. An example of moderate-intensity activity is brisk walking. One can spread these sessions out over the week and even do short, 10-minute spurts of activity 3 times a day on 5 or more days a week.

   Find ways to build short bursts of physical activity into day. While at work, take a 10-minute walking break or have a "walking," rather than a "sitting" meeting, if work and schedule permit. Use stairs instead of an elevator or escalator. Get off the bus one stop early. Meet a friend for a walk, instead of a meal.

4. **Myth: To lose weight, one has to give up all his/her favorite foods.**

   Fact: One does not have to give up all your favorite foods when they are trying to lose weight. Small amounts of favorite high-calorie foods may be part of one's weight-loss plan. Just remember to keep track of the total calories eaten. To lose weight, one must burn more calories than take in through food and beverages.

   Limiting foods that are high in calories may help to lose weight. A diabetes educator will help one to decide one's meal pattern, mode of physical activity and help to lose weight.

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, Nursing, Pharmacy, Occupational and Physiotherapy.

What is the duration of the course?

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

The Mentor can be selected from the particular locality and under whom the training can be done.

How will I get the course material?

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What are the course fees?

The standard fees 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.

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For further details visit helpdefeatdiabetes.org

MEMBERSHIP FORM

Association of Diabetes Educators (ADE)

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

Name …… Date of Birth: ……

Address ……

……

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*: ……

……

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

The details are as folllows:

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 2022 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- 2022" - 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, 2022 !!!!

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

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VALERA

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VALERA (Evogliptin Tablets 5 mg) Composition: Each tablet contains: Evogliptin hydro bromide hydrate equivalent to Evogliptin.....5 mg Therapeutic indications: For the treatment of type 2 diabetes mellitus as an adjunct to diet and Exercise to improve glycaemic control, when used as a monotherapy or in combination with metformin. Dosage and method of administration: The usual adult dosage is 5 mg of Evogliptin administered orally once daily. Use in Paediatrics: Safety and efficacy in paediatrics have not been established. Use in the Elderly: There were 119 elderly patients (22.6%) aged 65 years or older out of a total of 527 patients in the phase II and III clinical studies of evogliptin. The administration in elderly patients has not been fully investigated. Since the elderly generally have decreased physiological functions such as hepatic and renal functions, caution needs to be exercised during administration while monitoring the patient's condition. Contraindications: Evogliptin Tablets are contraindicated in patients with: • Hypersensitivity to the drug or any of its components • Severe ketosis, diabetic coma or pre-coma and type 1 diabetes Special warnings and precautions for use: 1) Heart failure: Caution should be exercised 2) Renal impairment: Evogliptin should be cautiously administered while monitoring the patient's condition. As there is no clinical experience of Evogliptin in patients with end-stage renal impairment requiring dialysis, administration of Evogliptin is not recommended in such patients. 3) Hepatic impairment: Caution should be exercised in such patients. 4) Acute pancreatitis: There is no report of acute pancreatitis in patients administered with evogliptin. 5) Use in Pregnant women: Use in pregnant women is not recommended. 6) Use in Nursing Mothers: Evogliptin should not be used in nursing mothers. Undesirable effects: The most commonly reported AE was Gastritis, Periodontitis, Nasopharyngitis, Erectile dysfunction, Dyspepsia, Arthralgia, Diarrhoea, Pruritus, sciatica, Hypoglycaemia, dyslipidaemia, elevated amylase or lipase levels General Precautions: 1) Concomitant administration with drugs known to cause hypoglycemia: Insulin secretagogues such as insulin or sulfonylurea may cause hypoglycemia. Thus, lowering the dose of insulin or insulin secretagogues may be required to minimize the risk of hypoglycemia in case of concomitant administration with evogliptin. 2) Severe and disabling joint pain Shelf-life: 36 months For more information refer full prescribing information.

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