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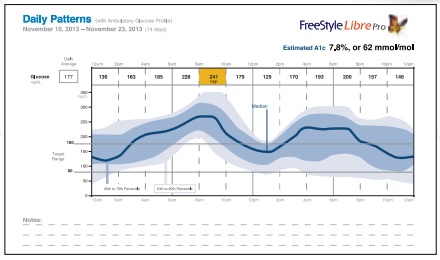

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CHILDHOOD OBESITY: NEW ETIOLOGY OF DIABETES MELLITUS

Raksha Goyal *

Introduction:

India is witnessing an increase in the burden of childhood obesity, especially among the upper socioeconomic strata and in urban areas. Emerging literature suggests a link between childhood obesity and the diabetes epidemic in India. Asian-Indian children and adolescents are increasingly susceptible to accumulate a high percentage of body fat and abdominal adiposity. Further, they are exposed to an obesogenic environment, created by rapid urbanization and nutrition transition. Obese children have a higher risk of developing abnormalities that are recognized as precursors to diabetes, such as subclinical inflammation, insulin resistance and metabolic syndrome, which often track extends into adulthood.

With a rapid demographic and socioeconomic transition, India is becoming the epicenter of epidemics of both adult and childhood obesity, especially in urban populations. Over the years, epidemiological studies have reported a consistent increase in the prevalence of childhood overweight and obesity in the subcontinent. A systematic analysis conducted as part of the Global Burden of Disease study 2013 reported that 5.3% of males and 5.2% of females aged less than 20 years in India were overweight. The overall prevalence of obesity among males and females in the above age category was 2.3% and 2.5% respectively.

Prediabetes and type 2 diabetes among children and adolescents in India

Globally, there has been an increase in the burden of prediabetes among children and adolescents. In a recent population-based study conducted in south India, the overall prevalence of dysglycemia was 3.7%, which increased to 12.7% in girls with abdominal obesity. The prevalence of impaired fasting glucose and impaired glucose tolerance among obese adolescents was 6.5% and 5.5% respectively.

Causes and Risk Factors of Childhood Obesity

Obesity is a multi-factorial condition. Various intrinsic and extrinsic factors may contribute to the risk of becoming obese. Among intrinsic factors a genetic predisposition and the hormonal situation can have a great effect on the individual risk to develop obesity during childhood. Since the last decade of the 20th century several genetic mutations that can cause obesity during childhood have been identified, furthermore the results of twin and adoption studies plead for a strong effect of genetic factors on the variation of the body mass index. From a physiological point of view hormones influence the development of obesity during childhood, on the other hand, adipose tissue is a source of a large number of obesogenic hormones. Hypothalamic or pituitary dysfunction results in altered hormone secretion. A decreased secretion of growth hormone, sex steroids or thyroid hormones is also associated with an increased risk of obesity. Another intrinsic factor contributing to childhood obesity is prenatal over-nutrition. It is assumed that maternal overweight increases the transplacental nutrient transfer, a condition which may result in permanent changes in appetite, neuroendocrine functions and metabolism. Another early risk factor for developing obesity during childhood is bottle-feeding. It could be shown that bottle-fed children had an increased risk to become obese in comparison to their breast fed counterparts. Beside these intrinsic factors the effects of extrinsic factors on the increasing prevalence of childhood obesity are discussed. Socioeconomic factors have a dramatic influence on the risk to become obese or not. Disadvantaged

* **Raksha Goyal,** Clinical and Sports Nutritionist, Joint Secretary, Indian Dietetics Association (M.P. Chapter), website: www.dietwindow.com • email: rakshagoyal20@gmail.com

groups characterized by a low socioeconomic status, poverty and a low educational level are at greatest risks for childhood obesity in industrialized countries. In these countries so called obesogenic environments prevail. An obesogenic environment is generally characterized by food security i.e. the physical, social and economic access to sufficient, safe and nutritious food, but also by reduced physical activity patterns and a sedentary lifestyle. Especially fatal consequences of an obesogenic environment are observable among populations in transition.

Acculturation and processes of modernization often result in the development of obesogenic environments. The result is the dramatically increase of obesity among populations in transition. This is mainly due to a change in eating habits and nutritional preferences. This means an increase in caloric intake and a decrease in physical activity. A comparable effect can be observed among children and adults with a background of migration. The analysis of the impact of migration or background of migration on childhood obesity is the topic of the present paper.

Childhood obesity and the pathogenesis of diabetes: evidence from India Subclinical inflammation

Inflammation is a key component of the link between obesity and diabetes. Longitudinal studies have established that obesity-associated chronic low-grade inflammation precedes and predicts diabetes. In obese children and adolescents, C-reactive protein (CRP) was the most consistent and the strongest association observed with inflammatory markers. Low levels of adiponectin, which are associated with insulin resistance and inflammation, have also have been observed in children and adolescents with obesity.

Insulin resistance

Childhood obesity is strongly associated with insulin resistance, which is considered as a forerunner of type 2 diabetes. Asian-Indian individuals are susceptible to insulin resistance from their early infancy. Further, insulin resistance syndrome has been reported in children as young as 8 years in India. Post-pubertal children in India reported a high prevalence of insulin resistance among children with adverse truncal body fat patterning, abdominal adiposity and excess body fat. 64% of the obese adolescents in India had fasting hyperinsulinemia, a surrogate marker of insulin resistance. Insulin resistance, measured in terms of values from the homeostatic model assessment of beta-cell function and insulin resistance (HOMA-IR), and increased progressively from normal weight to obese adolescents in both sexes. Early detection of insulin resistance among children is vital in the prevention of metabolic syndrome and diabetes.

Treatment

So the objectives of treatment should be "SMART" :

- **S**pecific
- **M**easurable
- **A**chievable
- **R**elevant
- **T**ime-bound

Here are few potential behaviors to target during treatment of childhood obesity

- Increase the amount of fruit eaten
- Increase the amount of vegetables eaten
- Increase the amount of whole grain cereals eaten
- Increase water intake and decrease high sugar drinks including fruit juice
- Eat breakfast every day
- Improve lunchbox contents
- Decrease i.e. food high in fat and/or sugar in lunchboxes and in after-school snacks
- Eat dinners that are lower in fat
- Eat fast foods less frequently
- Increase walking or cycling (and less car use)

- Increase involvement in informal physical activities (e.g. skateboarding, shooting basketball hoops)
- Increase participation in organized physical activities other than sport (e.g. dance, martial arts)
- Increase hours of physical education in schools
- Decrease TV viewing time
- Decrease electronic games time

Conclusion

Current literature suggests a high burden of generalized obesity among Indian children and adolescents, with a definite socioeconomic gradient. Asian-Indian children are increasingly susceptible to unfavourable body composition, as well as regional adiposity. The conventional BMI criteria for obesity are inadequate to identify these differences in body fat composition or distribution. Hence, ethnicity-specific, metabolically relevant cut-off values should be considered while diagnosing obesity and adiposity. Emerging literature suggests tracking of childhood obesity and body fat patterning to adulthood. Obese Indian children have a high burden of subclinical inflammation, insulin resistance and metabolic syndrome at a younger age than their non-obese counterparts.

Clinic-based studies from India, and migrant studies from high-income countries, report an increase in the proportion of type 2 diabetes among adolescents. The age at presentation of type 2 diabetes is also declining in India. All these point towards a direct link between childhood obesity and the diabetes epidemic in India.

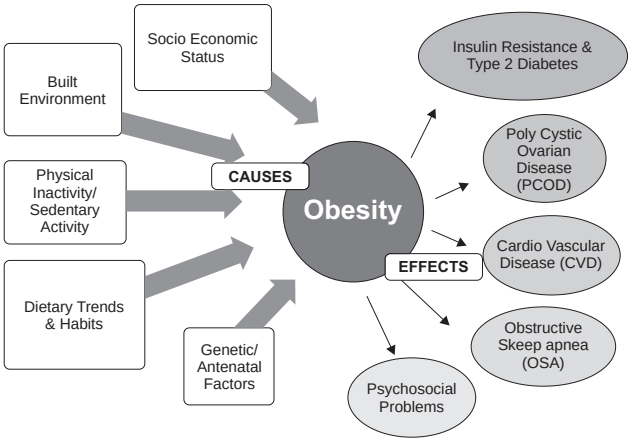

Figure: Childhood obesity-complex condition with multiple causes and consequences.

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ROLE OF EXERCISE IN DIABETES

Tasneem Navagharwala Ravat*

Introduction

Physical activity is any body movement produced by skeletal muscles that result in energy expenditure beyond resting expenditure. Exercise is defined as a physical activity that is planned, structured, repetitive, and purposeful, usually aimed at improving or maintaining physical fitness.

Physical activity has the potential to yield several health benefits for people with diabetes. These benefits can include improvements in glucose control, insulin sensitivity, lipid profile, blood pressure coagulation properties, body composition and psychological well being. Nearly everyone with diabetes can derive some benefit from an exercise program, although not all benefits will be realized by each person with diabetes. Both health care professionals and patients with diabetes need to remember this when determining the components of an exercise program. When chronic complications of diabetes develop, the benefits and risks of exercise must be carefully considered to maximize the benefits and assure safety.

Diabetes Mellitus

Diabetes is a group of chronic metabolic disorders characterized by hyperglycemia resulting from a relative deficiency in insulin through either reduced insulin secretion or reduced insulin action or both. The subsequent chronic hyperglycemia causes glycation of tissues, which almost inevitably leads to acute disturbances in metabolism and long term end organ damage and severe health complications.

The major forms of diabetes can be categorized as type 1 (T1DM) or type 2 (T2DM). In type 1, the cause is an absolute deficiency of insulin secretion resulting from autoimmune destruction of the insulin-producing cells in the pancreas. T2DM results from a combination of the inability of muscle cells to respond to insulin properly (insulin resistance) and inadequate compensatory insulin secretion. Less common forms include gestational diabetes (GDM), which is associated with a 40%-60% chance of developing T2DM in the next 5-10 year. Diabetes can also result from genetic defects in insulin action, pancreatic disease, surgery, infections, and drugs or chemicals.

Genetic and environmental factors are strongly implicated in the development of T2DM. The exact genetic defects are complex and not clearly defined, but risk increases with age, obesity, and physical inactivity. T2DM occurs more frequently in populations with hypertension or dyslipidemia, women with previous GDM, and non-Caucasian people including Native Americans, African Americans, Hispanic/Latinos, Asians, and Pacific Islanders.

Blood Glucose Control

- **At Rest**

At rest, muscle derives only —10% of its energy requirements from glucose oxidation, 85-90% from the oxidation of fatty acids, and 1-2% from amino acids.

- **During Exercise**

With the onset of exercise, glucose utilization increases rapidly. The initial response is a rapid

breakdown of muscle glycogen stores stimulated by activation of the sympathetic nervous system. Lactate accumulates rapidly and is released into the circulation. With continued exercise, blood flow to the muscles is increased, glucose uptake from the circulation occurs, and lactate release declines as aerobic metabolism is established. The increase in glucose uptake by exercising muscles is closely matched by increased

***Tasneem Navagharwala Ravat;** PhD Scholar; MSc RD, PG Dip; Email : tnavagharwala@gmail.com • Contact : +91 9833623962

hepatic glucose production, and blood glucose concentrations stay relatively constant. Hepatic glucose production is due predominantly to glycogenolysis with only —25% coming from gluconeogenesis.

The onset of exercise is also associated with the activation of lipolysis in adipose tissue and the release of free fatty acids (FFAs) and glycerol into the circulation. FFA concentrations rise and are taken up and utilized by exercising muscle in proportion to their concentration in plasma. Lactate, pyruvate, alanine, and other gluconeogenic amino acids released from muscle and glycerol released from adipose tissue are extracted by the liver and utilized for gluconeogenesis. These reactions are regulated by a complex but highly integrated system of neural and hormonal responses. Insulin secretion is inhibited by increased sympathetic nervous system activity via a-adrenergic receptors, and plasma insulin concentrations decline to low levels. This results in increased lipolysis in adipose tissue and increased hepatic glucose production.

Because exercise stimulates glucose uptake in muscle in the presence of very low concentrations of insulin, the fall in plasma insulin does not impair glucose utilization by working muscles or by other vital type II tissues such as the central nervous system. During exercise, plasma concentrations of glucose counter regulatory hormones increase gradually and play an important role in maintaining glucose homeostasis. These hormones include glucagon, growth hormone, cortisol, norepinephrine, and epinephrine. Glucagon plays a major role in stimulating hepatic glucose production, increasing both glycogenolysis and gluconeogenesis. Norepinephrine is important in stimulating glycogenolysis in both liver and muscle and in stimulating lipolysis in adipose tissue. Epinephrine increases in response to high-intensity exercise or declining blood glucose and has its major effect on hepatic glycogenolysis. Growth hormone and cortisol appear to be less important in the response to short-term exercise but do act to increase lipolysis, decrease insulin-stimulated glucose uptake in peripheral tissues, and increase hepatic gluconeogenesis over longer periods.

Type 1 Diabetes

In type 1 diabetes there is autoimmune destruction of the pancreas leading to a failure to secrete insulin. The aims of treatment for a diabetic now include mimicry of normal insulin levels throughout the day, achieving tight control, and prevention of microvascular and macrovascular complications.

Blood Glucose Control

Ambient insulin concentrations are vital in normal glucose homoeostasis both during exercise and in recovery. In normal subjects, plasma insulin concentrations decrease to low levels during exercise. This decrease, in conjunction with increasing plasma concentrations of glucagon and other counter regulatory hormones, promotes increased hepatic glucose production to match the increased rate of peripheral glucose utilization. The low insulin concentration during exercise also promotes lipolysis, making FFAs available for oxidation by exercising muscle and glycerol available to the liver for gluconeogenesis. In the insulin-treated diabetic patients, plasma insulin concentrations do not decrease during exercise and may even increase substantially if exercise is undertaken within an hour or so of an insulin injection. This effect is due to increased absorption of insulin from the subcutaneous tissue, particularly if the injection site is in an exercising part of the body. Enhanced insulin absorption by exercise is most likely to occur when the insulin injection is immediately before or within a few minutes of the onset of exercise. The longer the interval between injection and onset of exercise, the less significant this effect will be and the less important it is to choose the site of injection to avoid an exercising area.

Some diabetologists point out that there is considerable variation of insulin absorption rates from different injection sites such as

the thigh, abdomen, or arm and that this may have more of an effect on the rate of insulin absorption than the exercise itself. A good rule of thumb is to avoid vigorous exercise within 60-90 min of an insulin injection to minimize enhanced absorption. However, even with this precaution, plasma insulin concentrations do not fall normally during exercise in type I diabetic patients and glucose homeostasis may be impaired. The sustained insulin levels during exercise may enhance peripheral glucose uptake and stimulate glucose oxidation by exercising muscle. However, the major effect is an inhibition of hepatic glucose production. Both glycogenolysis and gluconeogenesis are inhibited by the high insulin levels and, even though counter regulatory hormone responses may be excessive, the hepatic glucose production rate cannot match the rate of peripheral glucose utilization, and blood glucose concentration falls. During mild to moderate exercise of short duration, this decrease in blood glucose concentration may be considered a beneficial effect of exercise, but during more vigorous or prolonged exercise, hypoglycemia may result. The risk of hypoglycemia is particularly high in some diabetic patients with glucagon deficiency, because both insulin and glucagon play major roles in the regulation of hepatic glucose production during exercise. Strategies to avoid hypoglycemia during prolonged, vigorous exercise include decreasing insulin dosage before exercise and taking supplemental carbohydrate feedings before and during exercise.

Effect of exercise and meal

The metabolic responses of people with type I diabetes to moderate-intensity exercise 30 min after breakfast have been studied and compared to those of normal subjects. In normal subjects the expected postprandial rise in blood glucose and insulin concentrations is rapidly reversed by exercise, returning to fasting levels within 45 min. When exercise is stopped, there are moderate rebound increases in glucose and insulin concentrations that do not exceed those occurring after breakfast alone. Thus, 45 min of cycle exercise started 30 min after a meal has a significant but transient effect to lower blood glucose concentrations.

In patients treated with subcutaneous insulin, responses to exercise started 30 min after breakfast have been found to be variable, with the majority having improved blood glucose concentrations that persist even through lunch. Some subjects, however, show improved glucose levels during lunch only and a few show no significant improvement at all. Thus, the effect of exercise after meals on blood glucose concentrations and the appropriate adjustments in insulin dosage may vary considerably, and individual responses should be determined to achieve improved glucose control and avoid symptomatic hypoglycemia.

Risks of Exercise in Type 1 Diabetes

Another major problem for the type I diabetic patient is the occurrence of post exercise hypoglycemia. Many diabetic patients experience increased insulin sensitivity and hypoglycemic reactions for several hours after exercise, in some cases even the next day. This residual effect is due to increased glucose uptake and glycogen synthesis in the previously exercised muscle groups, which is associated with increased insulin sensitivity and activation of glycogen synthase. Hepatic glycogen stores are also rebuilt after exercise, but at a slower rate than occurs in muscle, so that increased requirements for dietary carbohydrate may persist for up to 24 h after prolonged glycogen-depleting exercise.

A third problem encountered by type I diabetic patients occurs when exercise is undertaken during insulin deficiency. In this situation, plasma insulin concentrations are very low or absent, and hyperglycemia and ketosis are present. With the onset of exercise, peripheral glucose utilization is impaired, lipolysis is enhanced, and hepatic glucose production and ketogenesis are stimulated. These changes result in a rapid rise in the already elevated blood glucose concentration and the rapid development of ketosis. In other words, the already poor metabolic control rapidly

becomes worse, and instead of having a blood glucose-lowering effect, the exercise causes a rapid deterioration of the metabolic state. To avoid this deterioration, the diabetic patient should check his/her blood glucose concentration and urine ketones before undertaking vigorous physical activity. If blood glucose is >250 mg/dl and ketones are present in urine or blood, the exercise should be postponed and the individual should take supplemental insulin to reestablish good metabolic control. Likewise, if blood glucose is <100 mg/dl and the individual has taken insulin within the past 60-90 min, supplemental feedings should be taken before and during exercise to avoid hypoglycemia.

A checklist of factors to consider before the onset of exercise is provided in Table 1.

Table 1: Considerations before exercise

Type of exercise
Estimated intensity and duration of exercise
Estimated caloric expenditure
Is the exercise habitual or unusual?
How does the exercise relate to the level of physical conditioning?
Blood glucose
If < 100 mg/dl, take preexercise snack
If 100-250 mg/dl, all right to exercise
If >250 mg/dl, delay exercise and check urine ketones
Urine ketones
If negative, all right to exercise
If positive, take insulin; don't exercise until ketones are negative
Insulin
Type and dose
Time of injection
Site of injection
Food
Time of last meal
Preexercise snack
Carbohydrate feedings during exercise
Extra food after exercise

A number of strategies that may be useful to avoid either hypo- or hyperglycemia are outlined in Table 2.

Table 2: Strategies to avoid hypo- or hyperglycemia with exercise

Food
Eat a meal 1-3 h before exercise
Take supplemental carbohydrate feedings during exercise, at least every 30 min if exercise is vigorous and of long duration
Increase food intake ^24 h after exercise, depending on intensity and duration of exercise
Insulin
Take insulin >1 h before exercise
Decrease insulin dose before exercise
Alter daily insulin schedule
Blood glucose monitoring
Monitor blood glucose before, during, and after exercise
Delay exercise if blood glucose is >250 mg/dl and ketones are present
Learn individual glucose responses to different types of exercise

Type 2 Diabetes

In contrast to type I diabetes, in which deficiency of endogenous insulin is the primary defect, type II diabetes is characterized by insulin resistance and impaired insulin secretion but not total insulin deficiency.

Exercise helps to:

- Improve glucose control:
  - o Improving insulin sensitivity.
  - o Increasing GLUT4 (glucose transporter 4)
- Muscle uses more glucose, even at rest.
- Helps in weight lose.
- Improves physical fitness & reduces fat %.
- Improves CV (cardiovascular) function & CHD (coronary heart disease) risk profile.

Acute Effects of exercise

A. Fuel mobilization, glucose production, and muscle glycogenolysis.

The maintenance of normal BG at rest and during exercise depends largely on the coordination and integration of the sympathetic nervous and endocrine systems. Contracting muscles increase uptake of BG, although

BG levels are usually maintained by glucose production via liver glycogenolysis and gluconeogenesis and mobilization of alternate fuels, such as free fatty acids (FFAs).

B. Insulin-independent and insulin-dependent muscle glucose uptake during exercise.

There are two well-defined pathways that stimulate glucose uptake by muscle. At rest and postprandially, its uptake by muscle is insulin dependent and serves primarily to replenish muscle glycogen stores. During exercise, contractions increase BG uptake to supplement intramuscular glycogenolysis. As the two pathways are distinct, BG uptake into working muscle is normal even when insulin-mediated uptake is impaired in type 2 diabetes. Muscular BG uptake remains elevated postexercise, with the contraction-mediated pathway persisting for several hours and insulin-mediated uptake for longer.

Glucose transport into skeletal muscle is accomplished via GLUT proteins, with GLUT4 being the main isoform in muscle modulated by both insulin and contractions. Insulin activates GLUT4 translocation through a complex signaling cascade. Contractions, however, trigger GLUT4 translocation at least in part through activation of 5′-AMP–activated protein kinase. Insulin-stimulated GLUT4 translocation is generally impaired in type 2 diabetes. Both aerobic and resistance exercises increase GLUT4 abundance and BG uptake, even in the presence of type 2 diabetes.

Chronic effects of exercise

A. Metabolic control: BG levels and insulin resistance.

Aerobic exercise has been the mode traditionally prescribed for diabetes prevention and management. Even 1 week of aerobic training can improve whole-body insulin sensitivity in individuals with type 2 diabetes. Moderate and vigorous aerobic training improve insulin sensitivity, albeit for only a period of hours to days, but a lesser intensity may also improve insulin action to some degree.

B. Lipids and lipoproteins.

Blood lipid responses to training are mixed but may result in a small reduction in LDL cholesterol with no change in HDL cholesterol or triglycerides. Combined weight loss and PA may be more effective than aerobic exercise training alone on lipids.

C. Hypertension.

Aerobic training may slightly reduce systolic BP, but reductions in diastolic BP are less common, in individuals with type 2 diabetes.

D. Mortality and CV risk.

Observational studies suggest that greater PA and fitness are associated with a lower risk of all-cause and CV mortality.

E. Body weight: maintenance and loss.

Recommended levels of PA may help produce weight loss. However, up to 60 min/day may be required when relying on exercise alone for weight loss.

F. Supervision of training.

Individuals with type 2 diabetes engaged in supervised training exhibit greater compliance and BG control than those undertaking exercise training without supervision.

G. Psychological effects.

Potential mechanisms of exercise include psychological factors, such as increased self-efficacy, a sense of mastery, distraction, and changes in self-concept, as well as physiological factors such as increased central norepinephrine transmission, changes in the hypothalamic adrenocortical system, serotonin synthesis and metabolism, and endorphins. Regular PA may improve psychological well-being, health-related QOL (quality of life), and depression in individuals with type 2 diabetes, among whom depression is more common than in the general population.

Guidance for type 2 diabetes mellitus:

- May need to modify oral hypoglycemic regimen.
- Target of 20-60 minutes moderate intensity exercise at least 4 days per week.

- Couple exercise regimen with diet planning to optimize treatment.

Effect of Physical Activity on Blood Glucose

Depends on:

- **Physiologic Factors:** Status of Metabolic Control; Fitness Level; Blood Glucose at onset of Exercise; Insulin Resistance.
- **Pharmacolocic Factors:** Type of Insulin / Oral Hypoglycemic Agent; Site of Insulin Injection; Time of Insulin Injection.
- **Exercise Factors:** Timing of Exercise; Intensity of Exercise; Duration of Exercise; Type of Exercise; Frequency of Exercise.
- **Caloric Intake:** Timing of Pre-Exercise Meal; Caloric Content of Pre-Exercise Meal (Quantity and Type).

Guidelines for Exercise in Diabetes

Pre Exercise Evaluation

Before beginning an exercise program the individual with diabetes mellitus should undergo detailed medical evaluation appropriate diagnostic studies. This examination should screen for the presence of macro- and micro vascular complication that be worsened by the exercise program. Identification of areas of concern will allow one to design an individualized exercise prescription that can minimize risk to the patient. A careful medical history and physical examination should focus on the symptoms and signs of disease affecting the heart and blood vessels, eyes, kidneys, and nervous system.

- Blood pressure and heart rate responses are often blunted due to elevated resting heart rate.
- Painless S segment depression is common in diabetic patients.
- Diagnostic specificity of ST segment depression is often reduced (due to previous silent myocardial infarction, conduction abnormalities).
- Ambulatory ECG monitoring for silent ischemia may be helpful in some diabetic patients, but not recommended routinely.

Cardiovascular system

A graded exercise test may be helpful if a patient, about to embark on a moderate to high-intensity exercise program, is at high risk for underlying cardiovascular disease based on one of the following criteria:

1. Age 35 years
2. Type 2 diabetes of > 10 years duration
3. Type 1 diabetes of > 15 years duration
4. Presence of any additional risk factor for coronary artery disease
5. Presence of micro vascular disease (proliferative retinopathy or nephropathy, including microalbuminuria)
6. Peripheral vascular disease
7. Autonomic neuropathy.

Peripheral arterial disease

Evaluation of peripheral arterial disease PAD) is based on signs and symptoms, including muscle pain in calves, cold feet, decreased or absent pulses, atrophy of subcutaneous tissues, and hair loss.

Retinopathy

The eye examination is necessary for every diabetic.

Nephropathy

Specific exercise recommendations have not been developed for patients with incipient (microalbuminuria > 20 mg min albumin excretion or overt nephropathy 200 mg min). Patients with overt nephropathy often a reduced capacity for exercise, which leads have to self-limitation in activity level.

Peripheral neuropathy

Evaluation of peripheral neuropathy can be made by checking the deep tendon reflexes vibratory sense, and position sense.

Autonomic neuropathy

The presence of autonomic neuropathy limit an individual's may exercise capacity and increase the risk of an adverse cardiovascular event during exercise. Cardiac autonomic neuropathy

(CAN) may be indicated by resting tachycardia 100 beats per minute), orthostasis (a fall in systolic blood pressure >20 mm Hg upon standing), or other disturbances in autonomic nervous system function involving the skin, pupils, gastrointestinal or genitourinary systems. These individuals may have difficulty with thermoregulation; they should be advised to avoid exercise in hot or cold environments and to be vigilant about adequate hydration.

Exercise Prescription

The exercise prescription must address recommendations on intensity, type, duration, frequency, and rate of progression of physical activity based on the findings of careful evaluation.

Intensity

It is frequently recommended that heart rate be used to determine the intensity of exercise. Instead, careful attention should be given to a patients subjective feelings of intensity using the rating of perceived exertion (RPE) scale (Table 3). The exercise intensity is prescribed according to the numerical values associated with corresponding adjectives subjectively describing intensity. It is recommended that the patients strive to reach a moderate-range RPE (-3) gradually over 2-4 weeks. lt is important that health care professionals clearly explain the RPE scale and emphasize its reliance on patients subjective feelings. Exercise should be terminated if a patient is unable to continue talking or if pedaling, to maintain a consistent pedaling frequency.

Table 3: Rating of perceived exertion

RPE	Scale
0	Nothing at all
0.5	Very, very weak
1	Very weak
2	Weak
3	Moderate
4	Somewhat strong
5	
6	Strong
7	
8	Very strong
9	Very, very strong
10	Maximal

Type

A patient's interest level should be what primarily drives the type of activity selected. It is important, however, that the person with diabetes and the health care professional give careful consideration to the ease of access and ease of performance indices when selecting the most appropriate types of activities. Activities that should be encouraged in this population are stationary cycling, semi-recumbent cycling, and water exercises. Water activities and semi-recumbent cycling are especially beneficial for those with orthostatic hypotension, since the pressure of water surrounding the body and the semi-recumbent posture respectively help maintain blood pressure sitting in a chair doing light resistance exercises (e.g. lifting light weights or using an elastic exercise band) may help maintain or increase muscle strength.

Rate of progression:

Any increase in intensity, duration and frequency should be small and approached cautiously to minimize risk of any dangerous cardiovascular events, musculoskeletal injuries, and/or relapse.

Conclusion:

In the context of diabetes, it is becoming increasingly clear that the epidemic of type 2 diabetes sweeping the globe is associated with decreasing levels of activity and an increasing prevalence of obesity. Thus, the importance of promoting physical activity as a vital component of the prevention as well as management of type 2 diabetes must be viewed as a high priority. It must also be recognized that the benefit of physical activity in improving the metabolic abnormalities of type 2 diabetes is probably greatest when it is used early in its progression from insulin resistance to impaired glucose tolerance to overt hyperglycemia requiring

treatment with oral glucose-lowering agents and finally to insulin.

For people with type 1 diabetes, the emphasis must be on adjusting the therapeutic regimen to allow safe participation in all forms of physical activity consistent with an individual's desires and goals. Ultimately, all patients with diabetes should have the opportunity to benefit from the many valuable effects of physical activity.

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VITAMIN D AND DIABETES

Khushboo Pathak*

Vitamin D is well known for its significant role in calcium homeostasis & bone metabolism. Recently, several studies have shown the importance of vitamin D in prevalence of many diseases and disorders like rickets, osteoporosis, cardiovascular diseases, diabetes, cancer and tuberculosis in India.

Vitamin D is synthesized by the body on adequate exposure of skin to sunlight which has Ultra Violet B (UVB) rays. These UVB rays are absorbed by 7-dehydrocholesterol in the skin, which is converted to previtaminD3. Previtamin D3 is then converted to vitamin D3. Vitamin D3 is then metabolized in the liver to form 25-hydrovitaminD3. In kidney, 25-hydrovitaminD3 is then converted to its biologically active form 1, 25-dihydroxyvitamin D3. Maximal synthesis of vitamin D on skin exposure to sunlight is seen between 11.00 a.m. to 2.00 p.m. during the entire year. Study says, ten minutes of sunlight exposure three times a week between 11.00 a.m. to 2.00 p.m. along with vitamin D supplementation is enough to maintain vitamin D levels.

Vitamin D level in the body is categorized as: +deficient<20 ng/mL, insufficient 20-29 ng/mL, sufficient 30-100>ng/mL&toxic>100 ng/mL. Diet, sunlight and commercial supplements are the sources for vitamin D. Vegetarian source for vitamin D includes milk but it hardly has enough vitamin D (2 IU/100 mL) unless it is fortified. And more options are available in non-vegetarian sources like egg yolk, cod liver oil and fatty fishes like salmon, tuna & mackerel. However, the content of vitamin D in above foods is not enough to maintain the levels of vitamin D. Also, boiling or cooking food for a long period can degrade vitamin D as it remains stable only up to 200°C. A study shows commercial supplementation of D3 is 87% more effective in maintaining and raising the serum concentration of 25-hydoxyvitamin D4, 25-hydroxyvitamin D is the most reliable marker of vitamin D and is measured in usual blood testing.

Deficiency of Vitamin D is largely seen in Indians irrespective of their age, gender, race, geography& diverse dietary practice. Studies have shown that 70-100 % adults & 85-98% school going children in India are at risk of vitamin D deficiency. Major causes are lack of exposure to sunlight, atmospheric pollution, skin pigmentation, indoor activity or indoor work, high rise buildings, and use of sunscreen to protect skin from sunlight.

Diabetes is an endocrine disorder associated with micro-vascular and macro-vascular morbidity and mortality if not controlled optimally. Vitamin D deficiency is linked with glucose intolerance and obesity by causing pancreatic beta cell dysfunction, impaired insulin action & systemic inflammation. Low vitamin D level is seen with an increase in adiposity & visceral fat.

Several studies have shown that vitamin D plays a major role in glucose metabolism. Vitamin D has a direct association with type 2 diabetes. Vitamin D deficiency can predict hyperinsulinemia. Hyperinsulinemia is linked with obesity, impaired blood glucose, hypertension & dyslipidemia.

Vitamin D deficiency increases insulin resistance. Insulin resistance is a major factor in pre diabetes. Insulin resistance is a condition where large amounts of insulin is secreted by pancreatic cells to maintain blood glucose levels but it is ineffective at the target cells of skeletal muscle, liver & adipocytes. Insulin resistance confers 5 fold increase in the risk of developing diabetes1. Vitamin D is also suggested to have a role in calcium influx which may be essential for the

***Khushboo Pathak,** Registered Dietitian, Nurture Health Solutions as Healthcoach.

actions of insulin in skeletal muscles and adipose cells. Vitamin D can enhance the production of insulin &its sensitivity by improving the survival of islet cells. Vitamin D can also prevent death of islet cells in individuals with diabetes. This can gradually improve blood glucose & HbA1C in people with pre diabetes or diabetes. Study says, higher levels of serum 25-hydoxyvitamin D can reduce diabetes by 55%.

In individuals with impaired fasting blood glucose, supplementing them with 500mg calcium & 700IU of vitamin D reduced the rise of fasting glucose & slowed the progression of insulin resistance over a period of three years. Early correction of vitamin D levels in infants can reverse occurrence of type1 diabetes. A study even showed that a dose of 2000IU vitamin D per day reduced the risk of developing type1 diabetes by 80%.

Vitamin D deficiency and diabetes are increasing around the world. The association of vitamin D deficiency with prevalence of diabetes has raised an alarm to educate individuals. To keep track of its sufficiency, vitamin D should be tested at least once a year or as prescribed by the doctor.

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DIABETES AND HYPOGLYCEMIA

Shaival Chandalia*

Hypoglycemia is seen more commonly in patients with type 1 diabetes rather than in patients with type 2 diabetes. During this article, we will discuss the reasons for the same. Hypoglycemia which requires assistance of another person to recover is called as severe hypoglycemia.

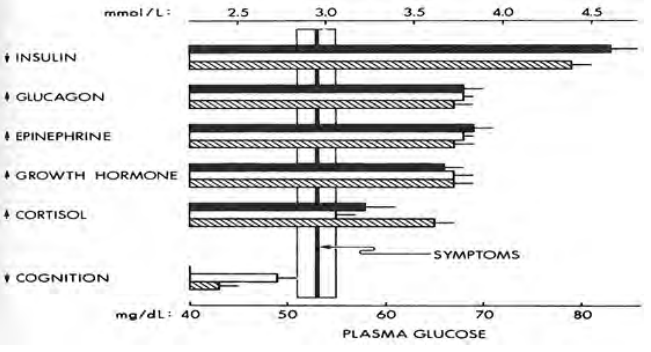
In the UKPDS, 3% of insulin treated type 2 diabetes experienced at least one episode of severe hypoglycemia per year. In the DCCT trial for type 1 diabetes, 10% of patients in the standard arm and 30% of patients in the intensive arm experienced at least one episode of severe hypoglycemia per year. Thus, although both were insulin treated there was a big difference in the incidence of severe hypoglycemia between type 1 and type 2 diabetes.

Hypoglycemia has become an important buzzword in diabetes literature. There is now evidence that hypoglycemia can worsen outcomes in certain situations. Apart from the catastrophic consequences of severe hypoglycemia which can result in unconsciousness or an accident while driving, adverse cardiovascular outcomes can occur specially in patients with long standing type 2 diabetes with/without cardiovascular disease. Hypoglycemia can acutely prolong the QT interval on the ECG. This can predispose to arrhythmias, resulting in adverse cardio-vascular outcomes. Hence, it is not advisable to control blood sugars very tightly in elderly patients with long standing diabetes. In a newly detected patient of type 2 diabetes, hypoglycemia is less likely to occur and and it is feasible to control blood sugars tightly. There is also something called the legacy effect, i.e early on in the natural history of type 2 diabetes, if one controls blood sugars well, the legacy of good glycemic control results in fewer complications later on, even if glycemic control is not as good later. So the take home message is that control blood sugars tightly in the initial years of type 2 diabetes and later on relax control.

Thus, hypoglycemia is just not an inconvenient reality of therapy for type 1 and type 2 diabetes, but it has adverse connotations for important outcomes such as heart attacks, strokes, death. Thus it becomes important to understand what is hypoglycemia and how does the body defend against hypoglycemia. Hypoglycemia is defined as a low blood glucose usually below 3.5mmol/ litre which is about 65mg/dl. THis threshold is not a hard and fast rule and it can shift upwards or downwards slightly. What is probably more important than the absolute number is the association of symptoms along with it. The symptoms of hypoglycemia include shaking, trembling, dizziness, sweating, palpitations, anxiety, jitteriness and if associated with a low blood sugar make the blood sugar level more clinically relevant.

Now the body's defense against hypoglycemia is multi- pronged.

Fig1: Thresholds for Counter regulatory responses



* **Dr Shaival Chandalia,** Endocrinologist & Diabetologist at Dr. Chandalia's Diabetes endocrine nutrition management and research center (DENMARC) and Jaslok and Bhatia Hospitals, Mumbai. Email Id: shaivalc@hotmail.com

Brain requires a continuous supply of glucose to function. An interruption of supply for as less as 3 minutes can cause brain damage or death, hence the body has a selfish stake in maintaining blood sugars as status quo and not allowing it to drift too low. As the blood sugar drops below 70mg/dl, the first defense against hypoglycemia is that insulin secretion from the pancreas is suppressed. As the blood sugar drops further glucagon secretion from the pancreas is increased. Then the third level of defense is that adrenaline and nor-adrenaline secretion is triggered. These are the so called fight or flight hormones. The effects of suppression of insulin secretion, stimulation of glucagon secretion and stimulation of adrenaline is to increase the blood glucose level.

The causes of mild hypoglycemia are due to absolute or a relative insulin excess. This can happen if a meal is missed or if excessive exercise is undertaken resulting in a mismatch between circulating insulin levels and requirements of insulin. But a more clinically relevant severe hypoglycemia is not due to these factors(like a missed meal or excessive exercise).

Fig 2 :Hypoglycemia in diabetes

- **Risk factors**

1 Absolute or relative therapeutic insulin excess

2 Compromised glucose autoregulation (risk factor for severe hypoglycemia)

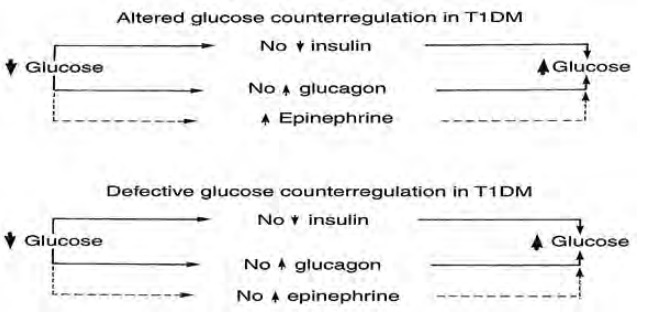
   a. absolute insulin deficiency(c-peptide negativity)

   b. h/o of severe hypoglycemia, hypoglycemia unawareness or aggressive therapy (lower HBA1c)

Most of the cases of severe hypoglycemia are due to other factors which is also the crux of the explanation as to why type 1 diabetics suffer from more hypoglycemia (severe hypoglycemia) than type 2 diabetics.

The causes of severe hypoglycemia are inadequate suppression of insulin, poor glucagon secretion and inadequate secretion of adrenaline.

Fig 3 : Defective counter regulation

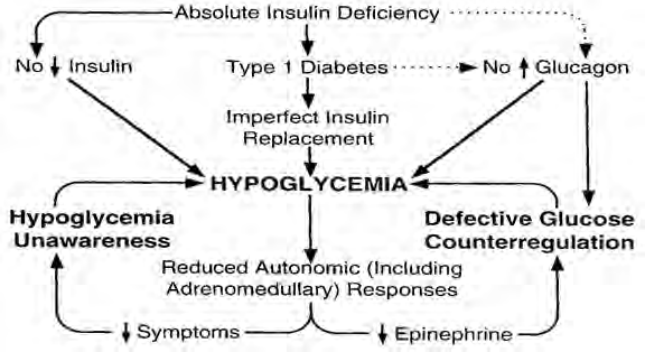


This happens largely due to loss of insulin producing beta cells in the pancreas of type 1 patients and long standing type 2 patients, as manifested by a poor C peptide level. Thus C peptide negativity or poor C peptide levels are responsible for inadequate suppression of insulin levels as the blood sugar drops. Also as beta cells are responsible for local signalling to the glucagon producing alpha cells in the vicinity,glucagon secretion is also suppressed. Hence the first and second lines of defense, suppression of insulin and secretion of glucagon are lost. This predisposes to severe hypoglycemia. Since type 1 patients have all their beta cells destroyed, C peptide is very low and hence, hypoglycemia is more frequent and severe. This is as opposed to type 2 diabetes, even those of long standing duration, have some C peptide production. C peptide is a surrogate marker of endogenous insulin secretion. Hence, poor C peptide predisposes to severe hypoglycemia as the first TWO lines of defense against hypoglycemia (reduced insulin secretion and stimulation of glucagon secretion) is lost. This is why type 1 diabetics are more prone to severe hypoglycemia than type 2 diabetics.

The situation is further exacerbated when the type 1 diabetic or long standing type 2 diabetic is tightly controlled. When the type 1 or insulin requiring type 2 diabetic is tightly controlled, the third line of defense against hypoglycemia, i.e secretion of adrenaline is lost. This is because the threshold for adrenaline release say at 50mg/dl drops to less than 40mg/dl.Before reaching 40mg/dl the patient is already drowsy and/

or unconscious. So he does not experience the characteristic symptoms of hypoglycemia like trembling, sweating, dizziness before he passes out due to neuroglycopenia. This condition is called hypoglycemia-unawareness, i.e the patient is not aware of hypoglycemia or does not feel the symptoms of hypoglycemia before it is too late.

Fig 4 : Hypoglycemia unawareness



This hypoglycemia unawareness increases manifold the risk of severe hypoglycemia and is dangerous, as the patient cannot take corrective measures, like ingestion of glucose, before lapsing into unconsciousness and coma. The symptoms that normally alert the patient to hypoglycemia are absent.

The best way to treat hypoglycemia unawareness is to relax control in type1 and long standing type 2 pateints. Even two weeks of relaxed control will restore the adrenaline response in such patients. As an extension of this, remember that the targets of blood glucose control in a type 1 and long standing type 2 diabetic should not be as stringent as a newly detected type 2 patient.

To summarize, we have talked about the adverse consequences of hypoglycemia. This is not a benign occurence that can be neglected. We then discussed the physiological defences against hypoglycemia and the role played by different hormones in that regard. We narrowed down on the reasons why type 1 diabetics are more prone to hypoglycemia than type 2 diabetics. Finally, we discussed the entity, hypoglycemia unawareness and how to avoid and/or treat it.

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WHAT'S NEW?

TYPES OF DIABETES

Shaival Chandalia*

Conventionally, two types of diabetes have been recognized. Type 1 diabetes primarily affects children (although it can be seen even in adults) and type 2 diabetes which primarily affects adults (but can also be seen in children). Hence, the conventional wisdom of type 1 affecting children only and type 2 diabetes affecting adults only, has changed.

Type 1 diabetes is due to autoimmune destruction of beta cells of the pancreas. This may be triggered by a virus or other environmental allergens. The clinical presentation of the illness is dramatic. Acutely, symptoms of increased urination, increased thirst and weight loss are seen. At times, presentation is more catastrophic with a condition called DKA i.e diabetic ketoacidosis. Here ketone bodies are produced as a result of fat break down. These ketone bodies are acidic in nature and cause the ph of the blood to turn acidic. Dehydration and respiratory hyperventilation to throw out acid through the lungs result in the classic presentation of DKA as a sick dehydrated child breathing rapidly. Type 1 diabetes can be seen in adulthood as well where the clinical presentation may be similar. However, DKA in an adult does not necessarily mean type 1 diabetes. A type 2 diabetic may present in adulthood as DKA when patient is under stress as is seen with an infection, a heart attack or stroke.

Just as type 1 can present in adulthood, type 2 diabetes is being seen more and more commonly in children. These children are usually overweight and have symptoms and signs of insulin resistance. Thus there may have blackening of the skin around the neck called acanthosis nigricans which is a sign of insulin resistance. It may be conjectured that being very overweight results in severe insulin resistance and the pancreas is unable to compensate which results in diabetes at puberty. It is fairly uncommon for these children to develop type 2 diabetes prior to puberty. Usually both the parents of such children have type 2 diabetes i.e there is strong family history. To be precise 70% of parents of such children are found to be having type 2 diabetes. Thus there is a strong polygenetic background on which is layered the insulin resistance of obesity resulting in diabetes. Weight loss is key to successful treatment but sometimes difficult to achieve. Metformin is a tried and tested drug in this situation although insulin may be required in the initial phase. The increasing prevalance of type 2 diabetes in children probably mirrors the epidemic of diabetes and obesity that we see in the adult population. This is mediated by easy availability of calorie dense foods and lack of exercise in our lifestyle. Industralization and coco- colonization are the drivers of this epidemic.

Now that we are familiar with the broad spread of diabetes in our populations, we can discuss other type of diabetes. There is an entity called latent autoimmune diabetes of adults or LADA. To define it in a nutshell, it could be called a slowly evolving type 1 or a fast evolving type 2 diabetes,i.e, it is seen in adults, above the age of 35 who are on oral tablets for at least 6 months after the diagnosis of diabetes, but progress fairly rapidly to insulin dependence. The other characteristic of these patients is that they have markers of autoimmunity which are

* **Dr Shaival Chandalia,** Endocrinologist & Diabetologist at Dr. Chandalia's Diabetes endocrine nutrition management and research center (DENMARC) and Jaslok and Bhatia Hospitals, Mumbai.

positive. Thus similar to type 1 patients they may have anti GAD and/or other antibodies which are positive. So the pathogenetic mechanism is through autoimmunity but the course is not as accelerated as type 1 diabetes. The term type 1.5 diabetes is often used to label this form of diabetes, as it is somewhat in between type 1 and type 2 diabetes, i.e it has characteristics of both. It evolves slower than type 1 but faster than type 2. Type 2 diabetes is characterised by insulin requirements after 10-15 years on average. But in LADA, insulin requirement is much earlier. The patients are usually lean as in type 1 diabetes although obesity may also be seen. There is no strong genetic predisposition as you see in type 2 diabetes.

As alluded to above, type 2 diabetes has a strong genetic predisposition. Type 2 diabetes in children has an even stronger genetic predisposition. Type 1 diabetes in children, adults will usually have a negative family history for diabetes. There is a small genetic predisposition depending on which HLA alleles are inherited but not a strong genetic background.

The genetic predisposition in type 2 diabetes is due to multiple genes. Hence the inheritance is called polygenic. Although a number of alleles have been identified, there is not a single gene which predisposes to type 2 diabetes. There are many genes, each with a little influence and the complex interactions between these multiple genes and the environment result in type 2 diabetes. In contrast, there is a type of diabetes called MODY or maturity onset diabetes of young. These are monogenic diseases i.e diabetes is caused due to a mutation in a single gene, as opposed to type 2 diabetes due to mutations in multiple genes. The inheritance of MODY is through an autosomal dominant route. If you are able to demonstrate genetic linkage through 3 generations in an autosomal dominant fashion in a young diabetic (less than 25) then MODY can be diagnosed in that family. These patients are usually lean but are antibody negative. There are about 14 types of MODY now identified and more are being identified all the time. Treatment can be oral tablets in some cases and insulin in others.

QUESTION AND ANSWERS

Q. WHAT ARE THE PSYCHAITRIC COMORBIDITIES IN PATIENTS WITH TYPE 1 DIABETES?

A. Diabetes mellitus as well as psychiatric disorders are common which may occur with one another and/or one may worsen the other. Psychological stress may follow screening for diabetes, as well as when diabetes is first identified. Patients with type 1 diabetes are at high risk of psychiatric disorders, which seems to be a consequence of the disease rather than due to a common familial etiology. At high risk are patients in mid-adolescence with comorbid disorders, low socioeconomic status or parental health problems. Type 1 diabetes mellitus contributes to the development of problems in parent–child relationships and employment difficulties, and negatively affects the quality of life. Psychiatric disorders in diabetic patients may account for 84% for mood disorders and 80% for anxiety disorders. Patients with diabetes are at an increased risk of developing substance abuse which accounts for 25-50% of patients leading to non-compliance with treatment and deterioration of diabetic control.

Patients with type 1 diabetes present with psychaitric disorders such as:

cognitive dysfunction, eating disorders, developmental disturbances, loss of consciousness, altered sensorium, depression, anxiety, inattention and hyperactivity, obsessive compulsive behavior, resilience, sleeping disturbances, schizophrenia, panic disorder, social phobia.

Cognitive dysfunction is characterized by a slowing of mental speed and a diminished mental flexibility, whereas learning and memory are spared.The magnitude of the cognitive deficits is mild to moderate, but even mild forms of cognitive dysfunction might hamper everyday activities since they can be expected to present problems in more demanding situations. Children with diabetes have a two-fold greater prevalence of depression, and adolescents up to three-fold greater, than youth without diabetes. Patients with type 1 DM may feel mild intermittent sadness, a longing for health, loneliness apprehension, or crankiness or irritability and may withdraw socially. Outbursts of temper, feelings of guilt, pessimism about the future, and refusal to attend school.

Management for patients with type 1 diabetes having psychaitric symptoms

Depressive symptoms have been linked to poorer disease management and glycemic control in adolescents with type 1 diabetes generating concern for multidisciplinary teams providing care to these adolescents.. Education should initially impart key information and help the patient and family grieve, so they can take up new challenges coming their way. Education should promote a sense that type 1 diabetes is compatible, with a healthy happy life style.

DIVYA JAIN

Q. WHAT ARE THE CAUSES OF TYPE 1 DIABETES IN CHILDREN?

A) The exact cause of type 1 diabetes is unknown. In people with type 1 diabetes, the body's immune system mistakenly destroys insulin-producing (islet) cells in the pancreas., which normally fights harmful bacteria and viruses. Environmental and genetic factors may play a role in this process.

The main function of insulin is to move glucose from the bloodstream to the body's cells. Sugar enters the bloodstream when food is digested. When the insulin producing cells gets destroyed, the child may produce little or no insulin at all.This may lead to

life threatening complications as the glucose builds up in the bloodstream.

Risk factors for type 1 diabetes in children include:

Family history - There is a slightly increased risk of developing type 1 diabetes if the parent or the sibling have this condition.

Genetic susceptibility. The presence of certain genes indicates an increased risk of developing type 1 diabetes due to general increase in developing autoimmune disease.

Race - Type 1 diabetes is more common among non- Hispanic white children than among other races in the United States.

Environmental risk factors might include:

Viruses - The autoimmune destruction of the islet cells is triggered by exposure to different viruses.

Diet - Early intake of cow's milk has been linked to increased risk of type 1 diabetes, whereas breast feeding might lower the risk. Another factor which affect the child's risk of type 1 diabetes is the timing of the introduction of cereal into the baby's diet. No specific nutrient has been linked to the development of type 1 diabetes in infancy.

DIVYA JAIN

Q. WHAT ARE THE SYMPTOMS OF TYPE 1 DIABETES IN CHILDREN?

A) Increased thirst and frequent urination: The fluid from the tissues is pulled into the blood stream when excess blood sugar builds up in the blood. Hence, the child might feel more thirsty and therefore drink and urinate more than usual. A young, toilet-trained child might experience bed-wetting suddenly.

- Weight loss: Unexplained weight loss is often the first sign of type 1 diabetes to be noticed in children. The child might lose weight, sometimes rapidly despite of eating more than usual to relieve hunger.
- Extreme hunger: Intense hunger is triggered when the muscles and organs lack energy as there is no sufficient insulin to move sugar into the cells.
- Irritability or behavior changes: The child might have poor performance in school and also may have mood problems. If the child further feels restlessness in addition to other symptoms, it could be a cause of concern.
- Fatigue: Lack of sugar in the cells might make the child feel tired and lethargic.
- Blurred vision: If the blood sugar levels are high fluid may be pulled from the lenses of your child's eyes, as a result the child may not be able to focus clearly.
- Fruity-smelling breath: Burning fat instead of sugar produces ketones that can cause a fruity breath odor.
- Yeast infection :Babies can develop diaper rashes caused by yeast. Girls with type 1 diabetes may have a genital yeast infections.
- Reduced blood pressure (falling below 90/60)
- Low body temperature (below 97º F)
- Rapid heart rate
- Changes to (or loss of) menstruation

Gastrointestinal (GI) symptoms:

- Nausea, abdominal pain, and change in bowel movements may be due to acute diabetic ketoacidosis.
- Acute fatty liver may lead to distention of the hepatic capsule, causing right upper quadrant pain.
- Persistent abdominal pain may indicate another serious abdominal cause of DKA (eg, pancreatitis).
- Chronic GI symptoms in the later stage of DM are caused by visceral autonomic neuropathy.

50% of patients with type 1 diabetes are affected by neuropathy, but symptomatic neuropathy typically develops after many years of prolonged hyperglycemia. Peripheral neuropathy presents as numbness, tingling and burning in both feet and at times hands as well.

Complications can include:

Heart and blood vessel disease: Diabetes may increase the child's risk of developing conditions such as coronary artery diseases with angina, atherosclerosis, heart attack, and high blood pressure later in life.

Kidney damage: Diabetes can damage the blood vessels that filter the waste from the blood. This severe damage can lead to kidney failure or irreversible end-stage kidney disease, which will require dialysis or a kidney transplant.

Nerve damage: Excess sugar can cause damage to the blood vessels that nourish the nerves, especially in the legs which may cause tingling, numbness, burning or pain. This happens gradually over a long period of time.

Skin conditions: Skin problems such as bacterial infections, fungal infections and itching may develop due to diabetes.

Eye damage: The blood vessels of the retina may get damaged due to diabetes, which may lead to poor vision and possibly can even cause blindness. it can lead to cataracts and increase the risk of glaucoma.

Osteoporosis: Diabetes may lead to lower than normal bone mineral density, increasing your child's risk of osteoporosis as an adult.

DIVYA JAIN

WHAT'S COOKING?

PALAK AND PANEER PARATHA

Ingredients :

INGREDIENTS	AMOUNT
Palak blanched	100 gm
Paneer grated	75 gm
Onion (finely chopped)	1
Ghee	2 tsp
Wheat flour	1 cup
Black pepper powder	1/4th tsp
Chaat masala	1/2 tsp
Red chilly powder	1/2 tsp
Jeera powder	1/2 tsp
Salt	To taste

Method of preparation :

1. Knead the wheat flour and prepare a soft dough. Keep aside for 10-15 minutes. Then apply few drops of oil and keep aside.
2. Blanch the palak leaves for 3-4 minutes, and then finely chop it.
3. In a bowl mix the chopped palak and all other ingredients.
4. Divide the dough into 3 parts and also divide the mixture into 3 portions.
5. Roll out a chapati and place the mixture in the center, spread the mixture properly and bring the edges of the chapati together and roll out evenly.
6. Place the paratha on a hot tawa and roast on both the sides. Apply ghee on both the sides and cook properly and serve.

Serves : 2

Nutritive value for 1 serving

Energy (kals)	Carbohydrates (gm)	Protein (gm)	Fats (gm)	GI
190	23 gms	7gms	6 g	Medium

DUDHI MUTHIYE

Ingredients :

FOR DHOKLA	AMOUNT
Bottlegourd (grated)	1/4 bowl
Wheat flour	1/2 cup
Besan	2 TBSP
Green chilly paste	2
Red chilly powder	1 tsp
Turmeric	1/4 tsp
Coriander powder	1/2 tsp
Oil	2-3 TSP
Coriander (chopped)	3 tbsp
Salt	To taste
FOR TADKA	
Mustard seeds	1 /2 tsp
Jeera	1/2 tsp
Onion (chopped)	1
Garlic	3-4 cloves
Green chilly (chopped)	2
Red chilly powder	1 tsp
Turmeric	1/2 tsp
Coriander powder	1/2 tsp
Salt	To taste
Coriander	1 tbsp
Curry leaves	6-7

Method of Preparation :

1. Mix all the ingredients for the dhokla and prepare a soft dough, divide into 3-4 parts.
2. Use oil and make thin rolls, place the rolls on the plate and then steam them in the steamer.
3. Steam for around 30 minutes. Then remove, let it cool and then cut them into small pieces.
4. For the tadka, heat oil in kadai, add mustard seeds, jeera add garlic, then chopped onions, once the onions turns translucent, add all the masalas, and then add the muthiya pieces and mix properly.
5. Add salt and coriander leaves and keep covered and heat on a low flame for 10-15 minutes.
6. Serve it either with kadi or curd.

Serves : 2

NUTRITIVE VALUE;

Energy (Kcal)	Carbohydrates (Gm)	Protein (Gm)	Fats (Gm)	Gi
325 kcal	55	10	15	Medium

MULTIPLE CHOICE QUESTIONS

1. Which ethnic groups are more likely to develop type-2 diabetes ?
   - Latinos
   - African – Americans
   - Caucasians
   - Pima Indians
2. Which of the following is not essential to assess the risk of an overweight /obese subject for developing type-2 diabetes ?
   - Body mass index
   - Waist circumference
   - Family history of diabetes
   - Birth weight
3. Which of the following is true about metabolic syndrome ?
   - Associated with lower body obesity
   - Associated with increased risk for diabetes mellitus and cardiovascular disease
   - Associated with type 1 Diabetes mellitus
   - Associated with Alzeimers Disease
4. Among female children and adolescents, the first sign of type-1 diabetes may be :
   - Rapid weight gain
   - Constipation
   - Genital candidiasis
   - Insomnia
5. Which region of the world has the highest incidence rates of childhood- onset type-1 diabetes ?
   - Africa
   - Asia
   - Eastern Europe
   - Northern Europe
6. Which of the following drugs is associated with clinical weight gain ?
   - Sibutramine
   - Pioglitazone
   - Pramlintide
   - Metformin
7. The essential fatty acids that must be derived from the diet are :
   - Stearidonic acid and eicosatetraenoic acid
   - Eicosapentaenoic acid and docosapentaenoic acid
   - Linoleic and alpha-linolenic acid
   - Gamma-linoleic acid and arachidonic acid
8. Common liver diseases in diabetes :
   - Hepatitis B
   - Hepatitis C
   - Non alcoholic steatohepatitis (NASH)
9. Type-1 diabetes is primarily due to the fact that :
   - The body fails to properly use insulin
   - The body does not produce insulin
   - The body is allergic to insulin
   - Low blood sugar
10. Drugs that block CHO or fat absorption :
    - Voglibose
    - Metformin
    - Glimepiride
    - Saxagliptin

ANSWERS:

1) Pima Indians : pima Indians have the highest prevelance of type 2 diabetes in the world. This is due to genetic factors with added environmental infuences.

2) Birth weight : Not the birth weight, but the current weight is an important indicator in assessing the risk of an overweight /obese subject for developing type-2 diabetes. Remotely, however the birth weight may determine the adult weight but here the question is trying top elicit the immediate proximal factor.

3) Associated with increased risk for diabetes mellitus and cardio-vascular disease - Metabolic syndrome is associated with increased risk of diabetes and cardiovascular disease. The other three factors have no connection with metabolic syndrome.

4) Genital candidiasis : High sugar levels lead to better conditions for the yeast to grow which tends to affect warm, moist areas of the body such as the vagina, penis, and certain areas of skin.

5) Northern Europe : The incidence of childhood onset diabetes is high in northern Europe as it accounts for about 20% of overall diabetes. In most other regions of the world it accounts only for 2-10% of diabetes.

6) Pioglitazone : This drug causes fluid retention and also increases the adiposity, hence, results in weight gain.

7) Linoleic and alpha-Linolenic acid : These fatty acids cannot be synthesized in the body and must be obtained from food. These basic fats, found in plant foods, are used to build specialized fats called omega-3 and omega-6 fatty acids.

8) Non-Alcoholic steatohepatitis – NASH is highly prevalent in type-2 diabetes,probably reflecting the frequent occurrence of obesity and insulin resistance in type-2 DM. Insulin resistance within the liver as well as extra hepatic tissues such as adipose and skeletal muscle is implicated in the pathogenesis of NASH.

9) The body does not produce insulin – Insulin is a hormone made by the pancreas that governs the metabolism of aa body fuels, primarily carbohydrates. Type 1 diabetics need life long insulin replacement therapy as endogenous insulin production is very low.

10) Voglibose : It delays the digestion of dietary polysaccharides by reversibly inhibiting carbohydrate digestive enzymes like sucrase, lactase, maltase.

MEMBERSHIP FORM

Association of Diabetes Educators (ADE)

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

Name ……..

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Work Experience: ……

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Currently employed at: ……

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Certificates attached regarding educational qualification and work experience:

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₹ 1000/- is payable in cash / cheque / draft with the application form

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BOOK REVIEW

RSSDI text book of Diabetes Mellitus; Editor-in-Chief: H B Chandalia, Executive Editor: G R Sridhar, Editors: A K Das, S V Madhu, V Mohan, P V Rao

Jaypee Brothers Medical Publishers; New Delhi; 2014; pages 1457; Price Rs 2995

The third edition of RSSDI Text Book of Diabetes Mellitus (D M) has been published six years after the second edition. It is authored and edited by those clinicians and professors who have been teaching and practising diabetes over many years within the country. A few chapters are contributed by Non-resident Indians. As pointed out by the editor-in-chief, this edition has undergone considerable revision. The material published both within the country and outside till the end of 2013 has been critically analysed and included. A few topics which are paid scant attention in other books, like-the complexity of insulin resistance, the criteria applicable to metabolic syndrome in Asians,challenges in the management of children and elderly with diabetes,musculoskeletal manifestation of diabetes, malnutrition modulated diabetes, Latent Autoimmune Diabetes in Adults (LADA), neonatal diabetes and the role of Yoga and relaxation techniques are unique to this book.

The flow chart on the management of diabetic ketoacidosis available in this book should be in possession of all ICUs. The colour pictures of retinopathy, foot lesions, skin diseases and musculoskeletal manifestation are well presented. The role of alternate therapy is extensively discussed. The guidelines for the beginner to organise a diabetic clinic and optimal health care for diabetes amidst diversity of social, economic and regional food habits is noteworthy. The limitation of stem cell therapy as of now is a good reminder. Some controversial issues are discussed in individual chapters. Much alike the chapter on A Glimpse in the Future, I wish a full chapter was devoted to controversies in diabetes. New chapters added in this edition are valuable and discuss important current issues. These include Sleep and Type 2 diabetes-mellitus, Early-onset Type 2 DM, Nutrient blockers and Bromocriptine, Insulin Pump Therapy, Glycemic Management in Hospitalized Patients, Continuous Glucose Monitoring System, Vitamin D and DM, HIV in Diabetes, Diabetes and Cancer.

The appendix is retained from the previous edition and gives a wealth of information applicable to Indian subjects like BMI and waist circumference and laboratory values in S I and conventional units.The index has attained perfection.The novel feature of this edition is mentioning the chapter number on the right edge of each page.

The book will prove to be valuable to students, physicians, diabetologists, endocrinologists and providers of diabetes care. It should be on the shelf of every medical library. The availability of this book has made the Western text books redundant. The single volume covering so many topics is bulky and heavy. I wish it was brought out in two volumes.

C. Munichoodappa. F.R.C.P.C.
Diplomate, American Board in Internal Medicine
Bangalore
Email id: dr.munichoodappa@gmail.com

JOIN US IN DIABETES PREVENTION PLAN

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WHY NOT ACT TOWARDS PREVENTING IT BEFORE ITS TOO LATE

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Colaba – 022-22840244
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(104, Lady Ratan Tata Medical Centre, M.Karve Road, Mumbai)

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25% insulin lispro (rDNA origin) injection
75% insulin lispro protamine suspension

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Humalog® mix50™ KwikPen™
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50% insulin lispro protamine suspension

ABRIDGED PRESCRIBING INFORMATION:

PRODUCT DESCRIPTION: Trulicity (dulaglutide) 0.75 mg/1.5 mg solution for injection in pre filled pen. **INDICATIONS AND USAGE:** Trulicity is indicated in adults with type 2 diabetes mellitus to improve glycaemic control as Monotherapy (The recommended dose is 0.75 mg once weekly) and Add-on therapy (The recommended dose is 1.5 mg once weekly). In monotherapy, when diet and exercise alone do not provide adequate glycaemic control in patients for whom the use of metformin is considered inappropriate due to intolerance or contraindications. Add-on therapy- In combination with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control. **CONTRAINDICATIONS:** Hypersensitivity to the active substance or to any of the excipients. **ADVERSE REACTIONS:** In the phase II and phase III studies conducted, 4,006 patients were exposed to Trulicity alone or in combination with other glucose lowering medicinal products. The most frequently reported adverse reactions in clinical trials were gastrointestinal, including nausea, vomiting and diarrhoea. In general these reactions were mild or moderate in severity and transient in nature. **USE IN SPECIFIC POPULATIONS:** For pregnancy, there are no or limited amount of data from the use of Trulicity in pregnant women. Studies in animals have shown reproductive toxicity. Therefore, the use of Trulicity is not recommended during pregnancy. For Breast feeding, it is unknown whether Trulicity is excreted in human milk. A risk to newborns/infants cannot be excluded. Trulicity should not be used during breast-feeding. The effect of Trulicity on fertility in humans is unknown. In the rat, there was no direct effect on mating or fertility following treatment with Trulicity.

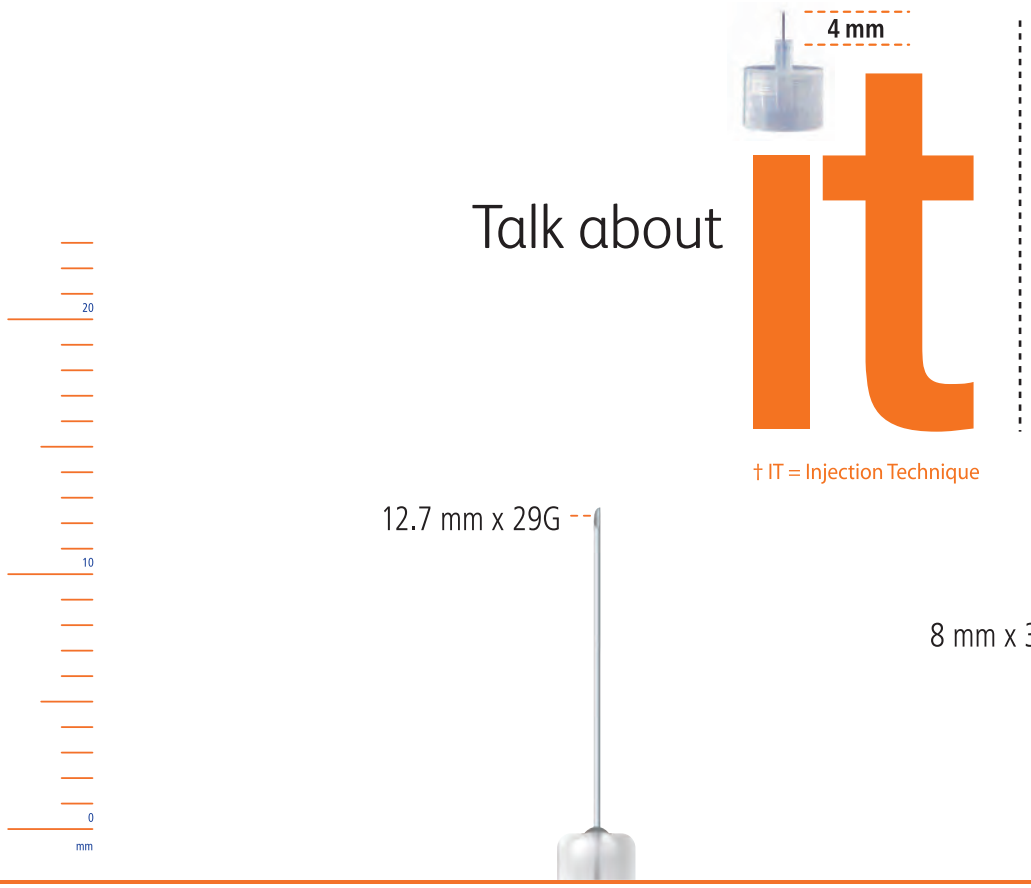
HUMALOG® 200 units/mL U-200 Abbreviated Prescribing Information

HUMALOG 200 units/mL U-200 is available as: • 3 mL Humalog KwikPen® (prefilled). **INDICATIONS AND USAGE:** HUMALOG 200 units/mL is a rapid acting human insulin analog indicated to improve glycemic control in adults and children with diabetes mellitus. **ROUTE OF ADMINISTRATION:** Subcutaneous Injection: HUMALOG U-100 or U-200. Administer the dose of HUMALOG U-100 or HUMALOG U-200 within fifteen minutes before a meal or immediately after a meal by injection into the subcutaneous tissue of the abdominal wall, thigh, upper arm, or buttocks. **DOSAGE INFORMATION:** Individualize and adjust the dosage of HUMALOG based on route of administration, the individual's metabolic needs, blood glucose monitoring results and glycemic control goal. Dosage adjustments may be needed with changes in physical activity, changes in meal patterns (i.e., macronutrient content or timing of food intake), changes in renal or hepatic function or during acute illness . Do NOT transfer HUMALOG U-200 from the KwikPen to a syringe for administration. Do NOT perform dose conversion when using either the HUMALOG U-100 or U-200 KwikPens. The dose window shows the number of insulin units to be delivered and no conversion is needed. Do NOT mix HUMALOG U-200 with any other insulins. Do NOT administer HUMALOG U-200 using a continuous subcutaneous infusion pump (i.e., insulin pump). Do NOT administer HUMALOG U200 intravenously. **DOSAGE FORMS AND STRENGTHS:** HUMALOG 200 units per mL (U-200) is available as: • 3 mL Humalog KwikPen (prefilled) **CONTRAINDICATIONS:** HUMALOG is contraindicated: • During episodes of hypoglycemia. • In patients who are hypersensitive to HUMALOG or to any of its excipients **UNDERSIRABLE EFFECTS/ADVERSE EVENTS:** Hypoglycemia is the most common adverse reaction associated with insulins, including HUMALOG. Severe hypoglycemia can cause seizures, may be life-threatening, or cause death. Hypokalemia All insulin products, including HUMALOG, cause a shift in potassium from the extracellular to intracellular space, possibly leading to hypokalemia. Untreated hypokalemia may cause respiratory paralysis, ventricular arrhythmia, and death.

HLG/Cycle Feb 2017/06

Consult the package insert for complete prescribing information.

Humalog® (Insulin Lispro I.P.), Humalog Mix25® Insulin Lispro Biphasic Injection I.P. (25% Insulin lispro and 75% insulin lispro protamine suspension) (100 IU/mL, 3 mL Cartridge) and Humalog® Mix50 Insulin Lispro Biphasic Injection I.P. (50% Insulin Lispro and 50% insulin Lispro protamine suspension) (100 IU/mL, 3 mL Cartridge) **INDICATIONS AND USAGE:** Humalog® is indicated for the treatment of patients with diabetes mellitus who require insulin for the maintenance of normal glucose homeostasis. **CONTRAINDICATIONS:** Humalog® is contraindicated during episodes of hypoglycemia. It is also contraindicated in patients with hypersensitivity to insulin lispro or any of the excipients contained in the formulation. **ADVERSE REACTIONS:** Hypoglycaemia is the most frequent undesirable effect of insulin therapy that a patient with diabetes may suffer. Severe hypoglycaemia may lead to loss of consciousness, and in extreme cases, death. No specific frequency for hypoglycaemia is presented, since hypoglycaemia is a result of both the insulin dose and other factors e.g. a patient`s level of diet and exercise. Local allergy in patients is common (1/100 to <1/10). Redness, swelling and itching can occur at the site of insulin injection. This condition usually resolves in a few days to a few weeks. **USE IN SPECIFIC POPULATIONS:** Data on a large number of exposed pregnancies do not indicate any adverse effect of insulin Lispro on pregnancy or on the health of the foetus/newborn. It is essential to maintain good control of the insulin-treated (insulin-dependent or gestational diabetes) patient throughout pregnancy. Insulin requirements usually fall during the first trimester and increase during the second and third trimesters. Renal and hepatic Impairment: Insulin requirements may be reduced in the presence of renal impairment.



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References:

1 Pen needle clinical study, conducted by Bruno and Ridgway among 143 diabetes patients, December2009.

2. Hirsch LJ, et al. Curr Med Res Opin 2010; 6: 1531-41. 3. Gibney MA, et al. Curr Med Res Opin 2010;26(6):1519-30.

* As at June 2017. #Patients aged 2–6 or extremely lean adults may require a pinch-up.

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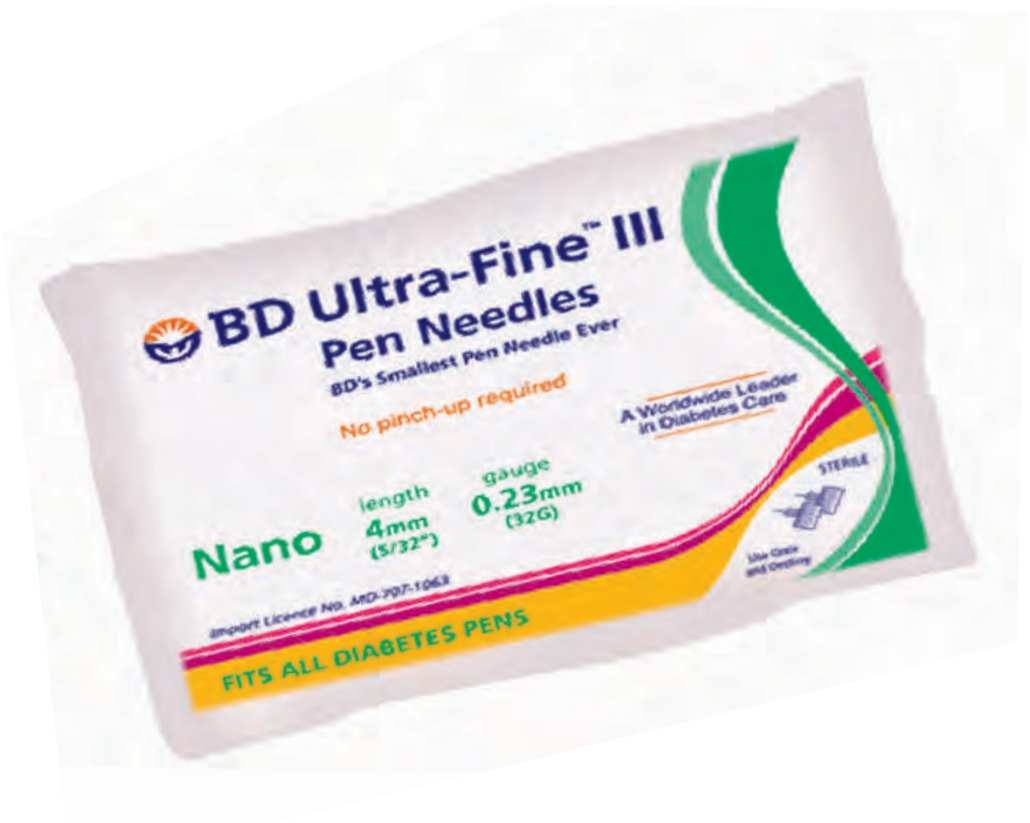

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References:
1. INVOKANA® India Prescribing Information (January 2014) **2.** Lavalle-González FJ et al. Diabetologia. 2013;56(12):2582-92 **3.** Cefalu WT et al. Lancet 2013;382(9896):941-50 **4.** Leiter LA et al. Diabetes Care. 2014. **5.** Stenlöf K et al. Diabetes Obes Metab. 2013;15(4):372-82.

For the use of a Registered Medical Practitioner or a Hospital or Laboratory Canagliflozin tablets 100mg / 300mg

INVOKANA®

Composition and Strength: Canagliflozin 100 mg / 300mg. Each 100 mg tablet contains 102 mg Canagliflozin hemihydrate, equivalent to 100 mg Canagliflozin. Each 300 mg tablet contains 306 mg Canagliflozin hemihydrate, equivalent to 300 mg of Canagliflozin. **Pharmaceutical form:** 100 mg - The tablet is yellow, capsule-shaped, immediate-release and film-coated, with "CFZ" on one side and "100" on the other side. 300 mg - The tablet is white, capsule-shaped, immediate-release and film-coated, with "CFZ" on one side and "300" on the other side. **Therapeutic Indications:** INVOKANA® is indicated as an adjunct to diet and exercises to improve glycemic control in adults with type 2 diabetes mellitus as monotherapy and combination therapy. **Dosage and Administration:** The recommended starting dose for adult > 18 years is 100 mg or 300 mg once daily orally preferably before the first meal of the day. A starting dose of 100 mg once daily should be used in patients on loop diuretics and patients ≥ 75 years of age. In patients with an eGFR 45 mL/min/1.73 m2 to < 60 mL/min/1.73 m2, the dose of INVOKANA® is limited to 100 mg once daily. The 300 mg dose may be considered for patients with an eGFR > 60 mL/min/1.73 m2, who need tighter glycemic control and who have a low risk of adverse reactions associated with reduced intravascular volume with INVOKANA® treatment. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. **Warnings and Precautions:** INVOKANA® has not been studied in pediatric patients (< 18 years), patients with type 1 diabetes and is therefore not recommended for use. INVOKANA® should not be used for the treatment of diabetic ketoacidosis or in patients with an eGFR < 45 mL/min/1.73 m2 [CrCl < 45 mL/min], as it would not be effective in these settings. In patients with evidence of reduced intravascular volume, correcting this condition prior to initiation of INVOKANA® is recommended. **Drug Interactions:** The metabolism of INVOKANA® is primarily via glucuronide conjugation mediated by UDP glucuronosyl transferase 1A9 (UGT1A9) and 2B4. If a combined inducer of these UGTs and drug transport systems (e.g., rifampicin, phenytoin, barbituates, phenobarbitol, ritonavir, carbamazepine, efavirenz) must be co-administered with INVOKANA®, monitor HbA1c in patients receiving INVOKANA® 100 mg once daily with consideration to increasing the dose to 300 mg once daily if additional glycemic control is needed. INVOKANA® neither inhibits cytochrome P450 CYP1A2, CYP2A6, CYP2C19, CYP2D6, or CYP2E1, CYP2B6, CYP2C8, CYP2C9, nor induces CYP1A2, CYP2C19, CYP2B6, CYP3A4 at higher than therapeutic concentrations. INVOKANA® is a P-glycoprotein (P-gp) substrate, and inhibits P-glycoprotein mediated transport of digoxin with low potency. Patients taking digoxin or other cardiac glycosides (e.g., digitoxin) should be monitored appropriately. **Pregnancy, Breast-feeding and Fertility:** There are no adequate and well-controlled studies in pregnant women. INVOKANA® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. It is not known if INVOKANA® is excreted in human milk. A risk to the breast-fed child cannot be excluded. The effect of INVOKANA® on fertility in humans has not been studied. **Adverse reactions:** In clinical studies of INVOKANA® the most commonly reported adverse reactions during treatment (≥ 5%) were vulvovaginal candidiasis, urinary tract infection, and polyuria or pollakiuria. Other adverse reactions in clinical studies of INVOKANA® that occurred at a rate < 2% in placebo-controlled studies were adverse reactions related to reduced intravascular volume (postural dizziness, orthostatic hypotension, hypotension, dehydration, and syncope), skin rash, and urticaria. In the event of an overdose, it is reasonable to employ the usual supportive measures, including monitoring of vital signs and observation of clinical conditions. **Overdose:** Single doses up to 1600 mg of INVOKANA® in healthy subjects and INVOKANA® 300 mg twice daily for 12 weeks in patients with type 2 diabetes were generally well-tolerated. In the event of an overdose, it is reasonable to employ the usual supportive measures, e.g., remove unabsorbed material from the gastrointestinal tract, employ clinical monitoring, and institute supportive treatment as dictated by the patient's clinical status. Canagliflozin was negligibly removed during a 4-hour hemodialysis session. Canagliflozin is not expected to be dialyzable by peritoneal dialysis.
Storage: Store below 30°C and in dry place. Protect from light. Keep out of reach of children.

Warning: To be sold by retail on the prescription of Registered Medical Practitioner only. Version: CCDS 09 Jan 2014
For complete prescribing information, please contact: Johnson & Johnson Private Limited, Arena Space, Behind Majas Depot, Off J.V. Link Road, Jogeshwari (E), Mumbai 400060

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