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Pharmacotherapy of Diabetes Mellitus Type 2: A Review on Various Hypoglycemics

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Abstract: Diabetes is a cosmopolitan medical issue ramifying a large population regardless of ethnicity. Elevated glycemic condition in a patient is explained as diabetes. It can be mainly categorized into Non-Insulin Dependent Diabetes Mellitus (NIDDM) and Insulin Dependent Diabetes Mellitus (IDDM) or Type 1 or Type 2 respectively. Type 1 or IDDM needs insulin therapy exclusively while Type 2 can be controlled via various hypoglycemic agents. Conventional classes contain glitazones, biguanides, sulfonylurea's and so on, while newly developed drug classes include gliptins or DPP-4 inhibitors, SGLT-2 receptor inhibitors and GLP-1 receptor agonists. The novelty in the anti-hyperglycemic agents have given promising results as compared to the conventional drugs. Insulin cannot be negated as far as its glycemic control is concerned. Furthermore, development of Insulin analogues like detemir, glargine, Lispro have been shown to control glucose levels in the plasma more efficiently.

Keywords: Pre-prandial; Postprandial; Ketoacidosis; Adipogenesis; Oral Hypoglycemic Drugs (OHD)

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1. Introduction

Diabetes Mellitus (DM) is a chronic disease rather a combination of symptoms with various co-morbidities which arises due to persistently increased plasma glucose levels. Diabetes is categorized mainly into Type 1 and Type 2 according to presence or absence of release of insulin [1]. In Type 1, there is complete cessation in release of insulin. The β-cells in Islet of Langerhans are destroyed by an autoimmune response. Therefore, there is complete absence of circulating insulin in the plasma which is to be compensated by administration of insulin exogenously. Meanwhile in Type 2 diabetes mellitus production of insulin is normal but problem lies in its activity which is hampered by insulin resistance due to obesity. That is why it is also called NIDDM (Non-insulin Dependent Diabetes Mellitus) [2].

Oral hypoglycemic therapy is the first line of treatment which involves the usage of sulfonylureas, glitazones, gliptins, biguanides and many more. However, at the later stage, insulin therapy has to be started inevitably as the symptoms of Type 1 start appearing [3].

In this review article, various pharmaco-therapeutic approaches for Type 2 diabetes mellitus have been discussed. Furthermore, a comparative account on various hypoglycemic has been outlined. Novel approaches for treating hyperglycemia have also been discussed.

2. Diabetes and its types

Diabetes Mellitus (DM) is a chronic disease, a syndrome or cluster of diseases pertaining to metabolism, detected by increased blood glucose level (hyperglycemia), which is the manifestation of defective insulin secretion, its activity or sometimes both. It has become a global health issue with increased morbidity, mortality along with health-related expenses [3]**.** In adults, the number of diabetic patients is thought to increase from 366 million up to 552 million by 2030 all around the world [4].

2.1. Type 1 DM

Type 1 Diabetes Mellitus (T1DM), previously termed as Insulin Dependent Diabetes Mellitus (IDDM), is characterized by complete cession of Insulin function and production from Islet of Langerhans or beta cells. This condition arises mainly due to an autoimmune response where antibodies are produced by the body against its own beta cells. Antibodies can also be produced against insulin, causing insulin dependent diabetes mellitus [5]. 5-10% of diabetic patients are diagnosed with T1DM [5, 6]. The outcomes of T1DM are ketoacidosis (as the first indicator), hyperglycemia which can aggravate in stress or in condition of an infection [7]. The progressive dysfunction of β-cells makes the patients dependent on insulin for the rest of his or her life. Though insulin is not the permanent remedy [8].

2.2. Type 2 DM

Type 2 Diabetes Mellitus (T2DM) was previously called Non-Insulin Dependent Diabetes Mellitus (NIDDM) and is a widespread and chronic disorder with a high percentage of 90-95% of diabetic patients diagnosed with it [7, 8]**.** It is diagnosed by irregularity in functioning of beta cells leading to decreased production of endogenous insulin along with insulin resistance, increased liver glucose irregularities and decreased levels of Glucagon like Peptide-1 [9]. There is rise of plasma glucose level in both pre-prandial (fasting) and postprandial (after taking a meal) conditions [9].

T2DM is found cosmopolitan, as one of the prominent health problems with high morbidity and mortality affecting 246 million people with a percentage of 6% and its prevalence is prognosticated to achieve 7.3 percent by 2025 of global population [10]. In another statistical analysis, the number of diabetic patients is predicted to hit 582 million by 2035. The patients range from children to adolescents of the whole globe. About 5.1 million mortalities in 2013 were due to diabetes [11]. According to the studies conducted by National Diabetes Information Clearing house and WHO, majority of patients are affected by type-2 diabetes. The prevalence of T2DM has increased to 22.9 % in 2013. In year 2011 the study showed a prevalence of 20.8 % [12].

3. Various classes of hypoglycemia

3.1. Sodium-glucose co-transporter-2 inhibitors

Sodium glucose co-transporter-2 (SGLT-2) inhibitors namely dapagliflozin, canagliflozin, and empagliflozin are the latest acknowledged hypoglycemic agents mainly used In USA and Europe [13, 14]. As far as its anti-diabetic mechanism is concerned inhibition of SGLT-2 pump in the renal vasculature inhibits the reabsorption of glucose in proximal convoluted tubule (PCT) leading to increased concentration of glycosuria (glucose in urine) which consequents in reduction of plasma glucose and glycosylated hemoglobin level [13].

Normally in a healthy and non-diabetic person 180 g of glucose is drawn back to the plasma from the glomerular filtrate [14]. Absorption of glucose is done by the presence of SGLT-1 and SGLT-2 transporters or carrier proteins in the renal tubules. SGLT-1 and SGLT-2 are membrane-bound insulin independent (not affected by insulin) protein moieties responsible for transporting glucose actively or against its concentration gradient. SGLT-2 is a potent glucose reabsorbing channel as compared to its isoform SGLT-

1. That is because SGLT-2 absorbs 90% of the glucose back into the circulation while remaining 10% is absorbed by SGLT-1. Location of SGLT-2 is exclusive and is present only in the early part of PCT, while SGLT-1 is present in the distal part of the convoluted tubule. It is also located in intestines where it renders same function of absorbing the glucose. In normal conditions, there should be no presence of glucose in the urine due to the presence of these glucose transporters. However, when the transporters are too saturated with glucose, the glucose will overflow into the urine [15]. The amount of glucose transportation (~350 mg/min) exceeds from the value and comes to a concentration range of 10–11.1 mmol/lit resulting glycosuria. The ability of glucose reabsorption by SGLT-2 and GLUT-2 is increased in diabetics resulting in hyperglycemia and decreased excretion of glucose [16].

SGLT-2 receptor antagonists as far as their comparative efficacy is concerned with other hypoglycemic agents, they not only improve glycemic control but also have auxiliary effects like weight loss, reduction in blood pressure (BP), decreased risk of hypoglycemia and optimizing cholesterol levels [14, 16]**.** SGLT-2 inhibitors exert their ability to reduce BP by limiting the reabsorption of Na^+ in the PCT leading to decrease in BP up to 4–6 mm of Hg/1–2 mm of Hg. While a weight reduction of 2.5 to 3 kg was seen after a year of initiation of therapy. There is a clinically insignificant small increase in plasma LDL and HDL and a slight decrease plasma triglyceride shown by drugs like dapagliflozin, canagliflozin, and empagliflozin. All SGLT-2 inhibitors are potent uricosurics showing 0.8–1.0% reduction in plasma uric acid**.** These drugs can be readily co-administered with other hypoglycemic including insulin [17].

3.2. Dipeptidyl peptidase-4 (DDP-4) inhibitors (Gliptins)

Gliptins is a new oral hypoglycemic class as compared to conventional drugs, used to cure type 2 diabetes patients. The group contains seven drugs namely Alogliptin, sitagliptin, vildagliptin, linagliptin, teneligliptin, anagliptin, and saxagliptin belonging to this class can be given alone as well as concomitantly with other classes of oral hypoglycemics like biguanides (metformin), glitazones (pioglitazone), sulfonylureas and insulin with a good therapeutic outcome [17]. Gliptins in combination with other hypoglycemic yield better results without risk of hypoglycemia and other side effects. This drug has shown good pharmacological (pharmacokinetic and pharmacodynamics) profiles in diabetic patients. Meanwhile reduction of dose up to 50%–70% is done in renal-compromised patients. It has shown no pharmacokinetic incompatibilities with drugs like metformin, pioglitazone, warfarin etc. [17, 18].

DDP-4 inhibitors are widely used hypoglycemic agents which have a good safety profile and decreased occurrence of hypoglycemia. Furthermore, they may avert the cardiovascular situations along with the prevention of atherosclerosis. These drugs might improve the standard of health. As far as the side effect profile is concerned DDP-4 inhibitors or gliptins have tolerable side effects like upper respiratory tract infections, headache and more if used in short-term whereas long-term usage may need further study. Although these medications may render side effects rarely but can be severe, like acute pancreatitis, anaphylaxis, angioedema and various allergic reactions**.** Pharmacodynamics involved in DDP-4 inhibitors is it actually exerts its anti-hyperglycemic effects by the inhibition of the enzyme dipeptidyl peptidase -4 enzyme responsible for cleavage of GLP-1, GIP along with various other peptides including natriuretic peptide released from brain. Inhibition of breaking down of GLP-1 results in prolongation omits activity which facilitates secretion of insulin. DDP-4 inhibitors increase the concentration of Incretins (an alimentary system hormone acting as an insulin secretagogue) [15, 18].

3.3. Glucagon-like peptide-1 receptor agonists

GLP-1 receptor agonists (GLP1RAs) are injectable hypoglycemic agents which control glycemic level in the blood by enhancing release of insulin, delaying gastric emptying, decreasing gastric secretion and inhibiting glucagon release. Gastric emptying and decreasing appetite occur due to action of the drug on

the central nervous system (CNS) and gastrointestinal tract. These drugs have good weight and appetite reduction ability and can be given with sulfonylureas [19]**.** These drugs have increased metabolic control in diabetics and also have achieved optimum glycemic control**.** GLP-1 agonists have rendered very fruitful outcomes when administered with insulin. A prospective study was initiated which included 125 patients suffering from T2DM having a body mass index of ≥ 35 kg/m^2. The interested outcomes for study were the effects on HbA1c, body weight, daily insulin dose and adverse reactions. The outcomes were periodically tested after three, six and 12 months. The outcomes were reduction of glycosylated hemoglobin and reduction in weight to a greater extent in first three months. After 12 months 14.3 kg of weight was reduced as well as the total doses of daily insulin were also reduced (−75.4 IU). 34% of diabetic patients terminated usage of insulin also. The conclusion of this study was that upon inclusion of a GLP-1 analogue along with insulin in an obese T2DM patient, positive outcomes in aspect of weight reduction and decreasing or stopping of insulin therapy can be achieved. Anyhow, no interrelation was found between weight reduction and HbA1c reduction [20].

The receptors of GLP-1 are located in the myocardial cells, vascular endothelium, arterial smooth musculature and kidney which corroborate the idea that they reduce cardiovascular risks. Through animal testing, GLP-1 agonists have shown cardio-protective properties by ameliorating glucose utilization, increasing left ventricular contractility, stroke volume and cardiac output. They also tend to decrease size of infarct in various animal models. Similarly in human studies it has shown lucrative effects on ischemic heart disease [19, 20]. As far as the side effect profile is concerned, GLP-1 agonists have been suspected to cause pancreatitis and developing tumors in thyroid and pancreatic tissue but several meta-analytical studies have negated the relationship between these drugs with carcinogenicity. Upon con-administration with exenatide, it has been reported to cause acute renal injury by causing nausea, vomiting and diarrhea. Commonly seen side effects are gastrointestinal (GI) upsets like nausea and headaches etc. these side effects are ruled out when the drug is discontinued. Moreover, it has no effect on cardiovascular system. These drugs are given as secondary options, concomitantly with such oral hypoglycemic agents which have weight gaining property like TZDs and Insulin and others [18, 20].

3.4. Insulin and its analogues

The insulin treatment has revolutionized the course of diabetes. Contemporary developments in DNA recombinant technologies and genetically feats have yielded new insulin alternatives achieving improved glycemic control, pharmacokinetics etc. Insulin Pumps and pens have assisted in improving patient adherence and compliance with the therapy. However, there is a need to develop various other insulin formulations like oral insulin which are in various stages of clinical trials [21].

Insulin administration is the primary treatment component in T1DM or juvenile diabetes where complete cessation of insulin production is seen. On the other hand, insulin is not considered as the first line treatment of T2DM but a majority of patients in the long run need insulin therapy to control glycemic condition. The need of exogenous insulin is necessitated by the insufficient secretion or development of resistance, eventually leading to complete exhaustion of β-cell and making insulin therapy inevitable. Eventually 30% of such types of patients need insulin therapy, Age, obesity and lack of physical activity can develop Type-2 diabetes. Sometimes 50% of patients initiate insulin therapy. Early initiation of insulin therapy can supplement the weakened function of β-cells along with controlling hyperglycemia [17-20].

Insulin therapy can rectify or optimize several T2DM associated anomalies like Insulin has been repeatedly reported to lower micro and macro vascular complications involving retinopathy, nephropathy and neuropathy. Micro and macro vascular complications do arise due to increased blood glucose levels. Insulin prominently and effectively controls blood glucose level and reduces the incidence of these complications in both T1DM and T2DM. It also regulates obnoxious lipoproteins which are seen in Insulin

resistance. The role played by Insulin in controlling the hyperglycemic conditions is mediated by down regulating glycogenesis whilst enhancing glucose uptake in peripheral cells [21].

The anti-hyperglycemic action of Insulin is not free of side effects, which are mainly uncontrolled hypoglycemia and gaining of weight**.** Not only is weight gain (due to anabolic effect) a side effect but studies have revealed that insulin has poor glycemic control when administered alone or with another Oral hypoglycemic drug (OHD) and has shown higher percentage of cases needing ambulatory services to counteract hypoglycemia. Furthermore, co-morbidities were also seen while treating patients with insulin and had to go for serious treatments. A study done by Meneghini et al. unveiled some insulin analogues detemir, having good results concerned to good control of hypoglycemia with decreased chances of hypoglycemia and weight gain. In addition, the combination of subcutaneous isophane insulin and soluble insulin was commonly used protocol for the patients. A study done by Choi et al also showed that long term and continuous subcutaneous insulin infusion therapy in Type 2 diabetic patients proved to have optimized blood glucose control along with improved activity of β-cells [22].

3.5. Rapid-acting insulin analogues

Rapid acting analogues of insulin include lispro, aspart and glulisine which are available in market to treat diabetes. The foremost genetically engineered analogue of insulin is lispro which got approval for clinical administration in 1996 and structurally differentiates from normal insulin in the sequence of amino acids; at position 28 and 29, proline and lysine are reversed. This reversion makes the molecule to get absorbed rapidly, achieving a peak plasma concentration in a shorter time period [21]. In aspart insulin, the position-28 is occupied by aspartic acid instead of proline endowing this analogue the capacity to get absorbed twice rapidly as that of normal insulin while glulisine analogue differs from normal insulin due to substitution in two positions; at position-3, lysine substitutes asparagine while at position-29, glutamic acid replaces lysine [18].

3.6. Long-acting insulin analogues

Long-acting insulin analogues involve insulin glargine (traded as Lantus) and insulin detemir (traded as Levemir). In insulin glargine, the early long-acting analogue, there is a substitution of amino acids in both chains. In α-chain at position 21, glycine replaces asparagine while in β- chain two arginine amino acids are attached causing elongation of β-chain. Glargine acts as a long-acting analogue due to its decrease solubility at body pH causing its precipitation at the site of injection in sub cutaneous layer, which is a stable insulin hexamer. Furthermore, delayed dissociation and unfluctuating absorption into the plasma augments its longevity of activity up to 24 hours. Its time of activity is observed after two hours of injection. Its steady and stable plasma concentration makes this analogue to show less hypoglycemic issues [22, 23]. Detemir insulin is made by acylation of myristic acid at the position no 29 to the lysine amino acid in the β-chain while omitting the terminal threonine residues at position no 30 in the β-chain. Detemir has prolonged self-association and reversible-binding ability with albumin protein at the site of injection resulting in increased activity. Besides, the concentration of insulin is buffered by binding with albumin. Its pharmacological effects last for 17 hours with good control on weight gain and hypoglycemia [19]. Older versions of long-acting insulin analogues are not used now as they have repugnant absorption and peaks of activity that lead to hypoglycemia [20].

Insulin is not recommended by clinical health care personnel due to easily avertable issues in T2DM. Issues like Initiation of therapy, compliance and persistency, skill, confidence are the main areas where patient and health clinician has to be properly involved in achieving insulin therapy outcomes. Poor compliance by patients is the main reason clinicians are reluctant to initiate or intensify insulin as it will limit the achievement of effective outcome of insulin therapy. It has become important to solve the various

issues which limit the usage of insulin. As for the management of diabetes and to improve patient compliance and adherence, usage of Insulin pens can be a good method which improves adherence and yielding a good therapeutic outcome [19, 20]**.** Similarly, in case of elderly patients, insulin therapy is not commonly initiated due to uncontrolled hypoglycemia, ill concepts about insulin, painful route of administration, needing of expertise and complexity of regimen, continuous supply of drug, financial status. Moreover, the patients who need insulin therapy have to visit hospitals and the supply insulin in primary health care sector is not properly distributed creating difficulties for patients and health care personnel in acquiring insulin [23, 24].

3.7. Sulfonylureas

Sulfonylureas were found out in 1942 when a study conducted by Janbon et al. showed that some sulfonamides yielded hypoglycemic activities in test animals. Carbutamide was the first milestone drug to cure diabetes. It was then withdrawn from usage due to unwanted results on bone marrow. It was not until in 1960 that various sulfonylureas were available for usage. Sulfonylureas are classified into generations. The first-generation drugs like acetohexamide, tolazamidetol butamide and chlorpropamide are no longer in use as mostly second-generation drugs like gliclazide, glimepiride, glyburide glibenclamide and many more are more effective in controlling glycemic levels [25]. These drugs tend to increase the activity of β-cells by stimulating them to release insulin. In other words, they act as insulin secretagogues by activating a receptor anchored on β-cells. These drugs must be prescribed to those patients who have controlled weights or to metformin contraindicated patients in order to achieve an adequate glycemic control. Sulfonylureas show the best effects in controlling fasting hyperglycemia [23, 24].

Sulfonylureas can also be used as monotherapy and gives a good result if compared with metformin, in the reduction of glycosylated hemoglobin. The side effect seen are weight gain and hypoglycemia. But due to efficacy and economical point of view sulfonylureas are mostly recommended as a second choice of therapy in diabetic patients. In elderly patients due to reduction of functioning of β-cells sulfonylureas as insulin secretagogues are favorable options for increasing secretion of insulin. Due to impaired renal and hepatic function, polypharmacy, etc. there is a higher percentage of hypoglycemia which might need hospitalization. The drugs like glyburide and chlorpropamide are responsible for hypoglycemia furthermore gliclazide has proved to beneficial in patients with renal failure. Glipizide does not need dose alteration and hence is useful in patients with chronic renal issues with a dose of ranging from 2.5mg–15mg once a day. Gliclazide abolishes oxidative stress and inflammation helping vascular activity. The SU therapy should be started from a lower dose and by meticulously monitoring the hypoglycemic appearances usually single day dose is enough in achieving normo-glycemia. Patients with chronic diabetes where there is failure of β-cell production sulfonylureas may fail [20-23].

3.8. Biguanides

Metformin is a biguanide commonly used representative drug to cure type 2 diabetes mellitus in Canada and European Countries. It is used as first line therapy for diabetes due to its safety and cost effectiveness, which promotes peripheral glucose absorption, decreases resistance to Insulin and inhibits the process of gluconeogenesis by inhibiting the responsible enzymes and also potentiates Insulin receptor and transport and translocation action of GLUT-4**.** In other words, it acts as an Insulin sensitizer and can be used in combination with other OHDs like alpha-glucosidase inhibitors, glitazones, gliptins and as well as be solely administered and a dose of 200 mg/day should reduce levels of HbA1c by 0.8%–2.0% [25]. Insulin sensitizers like pioglitazone are good choices for patients with non-insulin dependent diabetes mellitus. The main side effect of this drug is that it causes lactic acidosis due to inhibition of gluconeogenesis or the conversion of lactic acid and other non-carbohydrate moieties into glucose, hence accumulation of lactic

acid is seen leading to lactic acidosis. The risk of lactic acidosis is seen in patients having renal or hepatic problems because Metformin is eliminated via kidneys. A single patient in 0.1 million people having metformin therapy with creatinine clearance value of < 30 mL/min can be treated using alkaline diuresis or intravenous infusion of sodium bicarbonate, hydration and monitoring. Side effects of metformin are mainly dose dependent, such as alimentary canal problems like diarrhea, vomiting etc. There has been a minute chance to cause hypoglycemia and does not affect the body mass, but reduces weight. The side effects are tolerable and should be monitored when there is renal failure and should not be given with drugs that alter kidney function like NSAIDs as interaction can occur. Metformin has also shown to cause deficiency of vitamin B-12 leading to various types of anemias and neuropathy [24-26].

Metformin has been proven to decrease CV problems which is attributed to signaling of the enzyme AMP influenced protein kinase endothelial nitric oxide synthase, responsible for giving cardio- protective effect and according to a study Metformin in monotherapy has shown promising results in alleviating CV complications and reduction of cardiovascular mortality and morbidities. Metformin depicts appetite reduction capability, mediated by the inhibition of release of leptin from brown adipocytes and has shown long term weight reduction benefits. It has given equivalent efficacies in both normal weight and overweight patients having T2DM with obesity. Women with insulin resistance in Poly Cystic Ovarian Syndrome (PCOS), metformin has optimized the process of ovulation. In epithelial cells metformin has exerted an inhibitory role as compared to Insulin and in general, metformin has been proven to lower the risk of cancers in patients having OHD therapy comparatively [26, 27].

3.9. Thiazolidinediones

Thiazolidinediones (TZD) is a class of hypoglycemic agents which exert their anti-hyperglycemic activity by reducing insulin resistance in peripheral tissues, decreasing hepatic glycogenesis and gluconeogenesis. The reduction in insulin resistance is achieved via activation of Peroxisome proliferator activated receptor gamma (PPAR-γ) receptors. The basic and prime function of PPAR-γ is showed to be regulation of glucose and lipid metabolism along with the synthesis of adipose tissue (adipogenesis). TZDs decrease the hepatic conversion of glycogen into glucose along with improving the effects of insulin. Levels of HDLs is increased while reduction of triglycerides is done [21-24]. They also alleviate the characteristics of Insulin resistance like dyslipidemia, hyperglycemia, hypertension, cardiovascular abnormalities, hyper-coagulation, vasculogenic issues like atherosclerosis, ultimately leading to alleviation and delaying of chances and progression of macro and micro vascular issue in diabetic patients. TZDs alone has good control on macro and micro vascular problems as compared to the combination of sulfonylurea and metformin. TZDs have also shown anti-tumor capabilities via pre-clinical studies as they can initiate an apoptotic cascade by increasing the tumor suppressing factor p53 and decreasing Bcl-2. It has also the capability of causing an arrest of cell growth, stopping cell differentiation and metastasis via ubiquitin-protease system and extracellular signal-regulated kinase pathway inhibition. Besides it has also been shown that TZDs decreased the chances of incidence of cancer up to 7% [27, 28].

As far as side effects of TZDs are concerned, these drugs have been associated with bone fractures, weight gain and fluid retention. Fluid retention is due to activity of Na^+ ions in the distal part of nephron. Which can be controlled by K-sparing diuretic [29-34]**.** Some specific types of cancers were associated with TZDs. It should be pointed out that exclusively pioglitazone has been linked with the risk of having bladder cancer. It has been evident that pioglitazone when administered to lab animals, has caused development of bladder cancer. Therefore, patients having a familial history of bladder cancer must be meticulously selective in deciding the drug [35-40]. TZDs have proved to be have drastic effects on the metabolism of bone tissue with documented studies of causing bone demineralization and increased risk of osteoporosis and the magnitude of severity of T2DM should be considered as T2DM is itself a risk factor in causing osteoporotic

fractures, so while administering TZDs bone mineral density should be monitored. TZDs can increase the chances of bone fractures in patients via various mechanism like the stimulation of PPAR-γ receptor which not only has anti-hyperglycemic effect but also affect bone marrow pluripotent mesenchymal stem cells. These cells have capability to differentiate into fat cells and bone forming cells (osteoblasts). Due to stimulation of receptor the pluripotent mesenchymal stem cells preferentially differentiate into adipocytes instead of osteoblasts hence the bone formation is hampered and chances of bone demineralization and fractures are increased [41, 42].

4. Conclusion

High prevalence of obesity and sedentary life style has contributed towards an increased number of diabetic patients. Patient education and lifestyle intervention designed to manage body weight and treat obesity are essential for all diabetic patients. Besides, the high prevalence of DM is generating a massive demand for anti-diabetic drugs and prompting pharmaceutical companies to invest much on research and development (R&D) for producing safe and effective medications for the treatment of diabetes mellitus. It is also predicted that by the year 2030, more than 70 % of people with Type 2 DM will reside in both in developed and developing countries. Hence, there is an urgent need for public health policies for the primary prevention of T2DM.

Disclosure statement

The authors declare no conflict of interest.

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