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REVIEW ON HEALTH-RELATED LIFE STYLE MODIFICATIONS ON TYPE 2 DIABETES AND PROVIDE THE PATIENTS EDUCATION

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ABSTRACT

India is the country that leads the world with the highest number of diabetic patients and is called the "Diabetes Capital of the World." According to the International Diabetes Federation's 2006 Diabetes Atlas, the number of people with diabetes in India is currently around 40.9 million, and by 2025 it is expected to increase to 69.9 million if preventive measures are not taken urgently. Aims and objective to evaluate the health-related life style establishment in Type II Diabetes Mellitus patients and to emphasize patient education. To assess problems in glycaemic control and educate, reinforce healthy lifestyle advice. Results: Data shows that 94.64% of patients were married and 5.36% were unmarried. Details of life style modifications advised to the patient are as follows: Early morning awakening, Brisk walking/light exercises for 30 min, Massage/swimming, Yoga, after lunch walking for 15 min and finally after dinner slow walking for 15 min. Patients were advised to sleep only 6-7 h during the night and avoid sleep during day time. Patients were totally prohibited to take sweet items, fried items, fast foods, meat, milk products, cold drinks, chocolates, alcohol substances, dry fruits, curd, pickles, potato, sweet-potato, bread, butter, fermented items, etc. The assessment was done with symptoms of type II Diabetes mellitus polyuria, polyphagia, polydipsia, weakness, always desire to occupy bed, blurring vision. Conclusion: Based on published literature study it can be concluded that life style modifications and dietary interventions are two important tools by which adequate glycaemic control can be obtained in previously diagnosed type-2 DM patients. Thus, these tools are useful in patients, who are on anti-diabetic medication, without proper control on glycemic index. Emphasize on patient counselling the patient should be instructed discontinue drugs immediately and report unexplained hyperventilation, myalgia, malaise, unusual somnolence or other nonspecific symptoms of early lactic acidosis. Warn to patients not to consume excessive amounts of alcohol while taking metformin. Instruct to patient not to change drug dosage without medical approval. Encourage to patient to report abnormal blood glucose levels and advise to patient no to take medications including over the counter (OTC), without medical approval.

Key words: Patient counselling, Life Style Modification and Type-2 Diabetic Patients.

INTRODUCTION

India is the country that leads the world with the highest number of diabetic patients and is called the "Diabetes Capital of the World." According to the International Diabetes Federation's 2006 Diabetes Atlas, the number of people with diabetes in India is currently

around 40.9 million, and by 2025 it is expected to increase to 69.9 million if preventive measures are not taken urgently [1]. The so-called "Asian Indian Phenotype" refers to certain unique clinical and biochemical abnormalities in Indians,

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which include increased insulin resistance, greater abdominal adiposity, that is, a higher waist circumference despite a lower body mass index (BMI), lower adiponectin, and higher sensitive C-reactive protein levels. This phenotype of Asian Indians makes them more susceptible to diabetes. The primary driver of diabetes is the rapid epidemiological transition associated with changes in lifestyle changes like nutrition, dietary patterns, and decreased physical activity, as evident from the high prevalence of diabetes in most of the population [2].

Treating diabetes may prevent some of its complications, but it does not usually restore normoglycemia or eliminate all the adverse events. The diagnosis of diabetes is often delayed until complications present themselves in many patients. Although current methods of treating diabetes remain inadequate, prevention is preferable. By observational studies and clinical trials of diet and exercise, type 2 diabetes was preventable, which is supported by many pieces of evidence. Diabetes mellitus is a chronic disease that occurs when the pancreas does not produce sufficient insulin or the body cannot effectively use the insulin it produces. This leads to an increased concentration of glucose in the blood (hyperglycemia) [3]. (OR)

The term "diabetes mellitus" describes a metabolic disorder of multiple aetiologies characterised by chronic hyperglycemia with disturbances of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action, or both. The effects of diabetes mellitus include long-term damage, dysfunction, and failure of various organs (WHO, 1999).

Types of Diabetes Mellitus

Type 1 Diabetes:

Insulin-dependent Diabetes Mellitus (β -cell destruction, usually leads to insulin deficiency), immunemediated, idiopathic

Type 2 Diabetes:

Non-insulin dependent Diabetes Mellitus (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with insulin resistance).

Gestational Diabetes mellitus- There are two main types of Diabetes mellitus (DM)

Type 1 DM- is caused by the inability to produce insulin in our body and requires the person to take insulin in the form of an injection or an insulin pump. This type was previously called "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes."

Type 2 DM- is caused by insulin resistance; a condition in which cells in our body fail to use the produced insulin properly, and sometimes it is also combined with an absolute insulin deficiency. This type was previously

called "non-insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes."

Type 2 diabetes mellitus-

The main mechanisms which are responsible for the development of type 2 DM in a person are Insulin resistance and abnormal insulin secretion [4].

Risk factors-

Type 2 Diabetes seems to be a more complex condition than type-1 diabetes because there is a combination of resistance to the actions of insulin in liver and muscle together along with impaired pancreatic β -cell function which leads to 'relative' deficiency in insulin.

Natural history of type 2 diabetes-

In the early stage of diabetes insulin secretion by the pancreatic cells will take the responsibility for progressive insulin resistance, causing hyperinsulinemia and the β cells are unable to compensate adequately and there will be rise in blood glucose levels, leading to hyperglycaemia. With further failure in β -cell function (type 2 Diabetes) there will be deterioration in glycaemic control and treatment requirements will be increased [5].

Insulin resistance- In order to maintain blood glucose levels normal range insulin resistance comes first and to increase insulin secretion also. However, in susceptible individuals the pancreatic β cells fail to sustain the increased demand for insulin and there will be progression in insulin deficiency. In patients with type 2 Diabetes excessive production of glucose will be there in the liver and under-utilisation of glucose will be there in skeletal muscle which results from resistance to the actions of the insulin. The main characteristic feature of type 2 Diabetes is that it is very often associated with other medical disorders, like visceral obesity, hypertension and dyslipidaemia. The primary cause of insulin resistance remains unclear but this is a major focus of current research [5].

Pancreatic β-cell failure-

In the early stages of type 2 Diabetes there will be only a moderate decrease in the total mass of pancreatic islet tissue. Deposition of amyloid will be the most common pathological change in type 2 DM An attractive, but as yet unproven, hypothesis to explain β -cell destruction in type 2 Diabetes is that "together with insulin a polypeptide amylin is also secreted, so that in the presence of insulin resistance the excessive demand for insulin secretion also results in the formation of excess amylin which forms insoluble fibrils of amyloid and ultimately destruction of β cells will be seen. In type 2 DM the number of β -cell will be typically decreased to 20-30%, α -cell mass is unchanged and there will be a rise in glucagon secretion, which may lead to hyperglycemia [6].

Genetic predisposition-

The important etiological factor was genetic predisposition in type 2 DM as shown by marked differences in susceptibility id different ethnic groups and through studies which involved monozygotic twins where the concordance rates for type 2 DM reach 100%. It has been estimated that offspring of individuals with type 2 DM have approximately 15% chance of developing the disorder [7].

Environmental factors-

Epidemiological studies provide evidence that type 2 Diabetes is associated with overeating, especially when it is combined with obesity and sedentary life style. However, the majority of middle-aged Diabetic people are obese, only a small number of obese people will have chance to develop this disorder. There will be a tenfold increased risk for developing type 2 DM in people who are having BMI>30 Kgm².

Other risk factors

Age-

Type 2 diabetes is principally a disorder of the middle-aged and elder people. In the UK, it affects 10% of the population who are over 65, and over 70% of all cases of Diabetes occur after the age of 50 years.

Pregnancy-

There will be decreased insulin sensitivity during normal pregnancy through the action of placental hormones and this affects glucose tolerance levels. The insulin-secreting cells of the pancreatic islets may be unable to meet this increased demand in women who are genetically predisposed to develop diabetes and it is termed as 'gestational Diabetes' and is defined as hyperglycaemia occurring for the first time during pregnancy [8].

Clinical presentation-

The common signs and symptoms which are seen in type2 DM are represented pictorially. In the below diagram as follows:

Complications-

There are 2 - types of complications: Macrovascular complications and Microvascular complications.

Macro vascular complications-

Coronary circulation (MI), Cerebral circulation (TIA, Stroke), Peripheral circulation (Claudication, Ischemia) [9]

Micro vascular complications-

Retinopathy (Impaired vision), Nephropathy (Micro albuminuria, Retinopathy (Impaired vision), Peripheral neuropathy (Sensory loss & Motor weakness),

Foot diseases (Ulceration & Arthropathy), Peripheral neuropathy (Sensory loss & Motor weakness) and Foot diseases (Ulceration & Arthropathy) [10].

Non-Pharmacological Management-

Overall aim of treatment is symptom relief and prevention or delay of complications by targeting normal blood glucose levels. Patients treated with diet/exercise or with addition of one or more categories of oral medications, with a combination of oral medications and insulin, or with insulin alone. Glucometers to self-monitor blood glucose (with less frequency than with T1D). Early detection and treatment of complications (at intervals recommended by national and international guidelines): eye exam, urine test, foot care, and specialist referral as Self-monitoring for signs/symptoms of hypoglycaemia (such as hunger, palpitations, shakiness, sweating, drowsiness and dizziness) and hyperglycaemia. Patient education about diet, exercise, and foot care. Physical activity promotes the weight reduction and improves the sensitivity of insulin thus lowering blood glucose levels. Together with dietary treatment, a programmed of regular physical activity and exercise should be considered for each person. Such a programmed must be tailored to the individual's health status and fitness. People should, however, be educated about the potential risk of hypoglycaemia [11]

PHARMACOLOGICAL AGENTS

Biguanides- Metformin suppresses hepatic glucose production, increases insulin sensitivity, enhances glucose uptake by phosphorylating GLUT-enhancer factor, increases fatty acid oxidation, and decreases the absorption of glucose from the gastrointestinal tract. And most used overweight commonly in and obese patients. Research published in 2008 shows further mechanism of action of metformin as activation of AMPactivated protein kinase, an enzyme that plays a role in the expression of hepatic gluconeogenic genes. Due to the concern of development of lactic acidosis, metformin should be used with caution in elderly diabetic individuals with renal impairment. It has a low incidence of hypoglycemia compared to sulfonylurea's [12].

SULFONYLUREAS-

They stimulate the endogenous insulin secretion; they carry a risk of hypoglycemia. Glyburide is associated with higher rates of hypoglycemia compared to Glipizide. Elderly patients with DM who are treated with sulfonylureas have a 36% increased risk of hypoglycemia compared to younger patients. Some of the risk factors for hypoglycemia are age-related impaired renal function, simultaneous use of insulin or insulin sensitizers, age greater than 60 years, alcohol abuse, caloric restriction, multiple medications or medications that potentiate sulfonylurea actions. Long acting sulfonylurea such as

glyburide should be avoided in elderly patients and use of short-acting Glipizide should be preferred.in DM patients [13, 14].

MEGLITINIDES-

Repaglinide and nateglinide are non-sulfonylurea secretagogues which act on the ATP-dependent K-channel in the pancreatic beta cells thereby stimulating the release of insulin from the beta cells, similar to sulfonylurea, though the binding site is different. Meglitinides have a rapid onset and a short duration of action (4-6 hrs.) and thus lower risk of hypoglycemia. Meglitinides are given before meals for postprandial blood glucose control. Metabolism of Repaglinide is done by the liver and very minimal amounts excreted through urine and thus adjustment of dose is not necessary in patients with renal insufficiency except those patients in end-stage of renal disease [15].

THIAZOLIDINEDIONES-

They are the first drugs to address the basic problem insulin resistance in type 2 DM patients Thiazolidinedione is an insulin sensitizer, selective ligands transcription factor peroxisomes proliferator-activated gamma.. class includes pioglitazone&rosiglitazone.Pioglitazone has given the importance than rosiglitazone because the restricted use of rosiglitazone recommended by Food and Administration (FDA) Due to cardiovascular events reported with usage of rosiglitazone. Pioglitazone use is not associated with hypoglycemia and can be used in cases of renal impairment and thus well tolerated in older adults. Its use can be limited in older adults with DM due to concerns regarding peripheral edema, fluid retention and fracture risk in women. In congestive heart failure of elderly patients. In patients with class III-IV heart failure pioglitazone is contraindicated.so it is avoided in treatment [16].

ALPHA-GLUCOSIDASE INHIBITORS-

Acarbose, Voglibose and Miglitol agents are most effective for postprandial hyper glycaemia and should be avoided in patients with significant renal impairment. Their usage is usually be in limited due to side-effects such as diarrhea and flatulence. These are the agents not widely been used to treat type 2 DM individuals but are likely to be safe and effective [17].

INCRETIN-BASED THERAPIES-

They are available for to treat type 2 Diabetes. Generally, use as monotherapy, as an adjunct to diet and exercise or in combination with oral hypoglycemic agents in adults with type 2 DM. Examples are Exenatide, an incretin mimetic, and Liraglutide. Glucagon-like peptide 1(GLP-1) analogues are the foundation of incretin-based therapies which are to target the previously unrecognized

feature of Diabetes Mellitus pathophysiology resulting in sustained improvements in body weight control and glycemiccontrol. There is no risk of hypoglycemia with the use of GLP-1 therapies.when combined with insulin secretagogues shows the risk of hypoglycemia. In addition, they may have a positive impact on hepatic and cardiovascular health, sleep, inflammation, and the central nervous system [18].

DIPEPTIDYL-PEPTIDASE-4 INHIBITORS-

Dipeptidyl-peptidase (DPP) IV inhibitors inhibit the dipeptide peptidase-4 (DPP-4), a ubiquitous enzyme rapidly inactivates GLP-1 and GIP, and increase the active levels of these hormones and, also shows the improvement of islet function and glycemic control in type 2 DM. They are effective as monotherapy in patients inadequately controlled with diet and exercise. And combination with metformin, thiazolidinedione, and insulin can be used for more effectiveness. They carry a low risk of producing hypoglycemia. The long-term durability of effect on betacell morphology and on glycemic control function remains to be established [19].

INSULIN-

Insulin is used alone or in combination with oral hypoglycemic agents. Insulin comes in inject able forms rapid acting, short acting, intermediate acting and long acting. The long acting forms are less likely to cause hypoglycemia compared to the short acting forms. If some beta cell function remains the Augmentation therapy with basal insulin is useful. Basal-bolus insulin replacement is necessary if beta cell exhaustion occurs. In case of glucose toxicity their Rescue therapy using replacement is necessary which should mimic normal release of the insulin by beta cells of the pancreas [20].

INSULIN ANALOGUES-

Insulin therapy has ability to mimic normal physiologic insulin secretion. The pharmacokinetic profiles of the new insulin analogues are distinct from the regular insulin, and their onset and durations of action range from rapid to prolonged. Traditional intermediate- and long-acting insulins (NPH insulin, Lente insulin, and ultralente insulin) are limited by inconsistent absorption and peaks of action that may result in hypoglycemia. Currently, two rapid-acting insulin analogues, insulin lispro and insulin aspart, and one long-acting insulin analogue, insulin glargine, are available [21].

FUTUREIN DRUG THERAPY INHALED INSULIN-

The inhaled form of rapidly acting insulin which became available in 2006, after it was approved by both the European Medicines Evaluation Agency and FDA for treatment of type 1 and type 2 DM in adults. It is a rapid acting form of insulin that was indicated for use in adults with type 1 and type 2 DM and has the advantage of

delivery directly into the lungs. Studies have however shown that inhaled insulin is as effective as, but not better than short acting insulin. It was withdrawn from the market by the manufacturer in October 2007 due to poor sales.

Bromocriptine-

Quick-release bromocriptine has recently been developed for the treatment of type 2 DM. However, the mechanism of action is not clear. Studies have shown that they reduce the mean HbA1c levels by 0.0% to 0.2% after 24 weeks of therapy.

Others-

Inhibitors of 11ß-hydroxysteroid dehydrogenase 1, which reduce the glucocorticoid effects in liver and fat and Inhibitors of the sodium-glucose transporter 2, increase renal glucose elimination, pancreatic-G-protein-coupled fatty-acid-receptor agonists and Insulin-releasing glucosidase activators, glucagon-receptor antagonists, and metabolic inhibitors of hepatic glucose output are being assessing for the purpose of developing the new drug therapy for type 2 diabetic patients [22].

AIM & OBJECTIVES

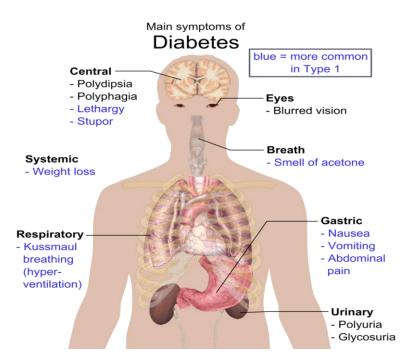
To evaluate the health-related life style establishment in Type II Diabetes Mellitus patients and to emphasize patient education.

To assess problems in glycaemic control and educate, reinforce healthy lifestyle advice.

INCLUSION CRITERIA:

- 1. All in patients and out Patients who are diagnosed as Diabetic type-II
- 2. Subjects with a past history of type II diabetes mellitus
- 3. And the patients previously having type II diabetes with improper glycaemic control even using oral anti Diabetic drugs.
- 4. Age of patients in between 25 and 75 years
- 5. Patients with diagnostic features of Type 2 Diabetes mellitus clinically such as polyuria, polyphagia, polydipsia, throat dryness, numbness/tingling hand and foot, weakness, always desire to occupy bed, sweating and sweet taste in mouth.
- 6. Continuing anti diabetic drugs (Metformin, Glibenclamide, Insulin, and Pioglitazone etc.), for their diabetes management.
- Fasting plasma glucose (FPG) level ≥120 mg/dl and/or
 2-h (postprandial) plasma glucose level ≥200 mg/dl.
 (8)
- 8. Who visit the hospital for 3months for check-up of disease?

Figure 1:



RESULTS

The present clinical study reveals that the age predominance of 46-65 years that is, 41.11% and then 25-45years, 66-85year were34.44, and 24.44% respectively.

Of 90 patients, 74.44% of the patients were males and 25.55% of patients were females. Out of 90 patients, maximum no of patients, that is, 35.55% are belonging to business category, and 24.44% are belongs to farmers 15%

patients were indulged in house hold work&15% belongs to labour. Data shows that 94.64% of patients were married Clinical improvement in and 5.36% were unmarried. signs and symptoms after dietary interventions and lifestyle modifications observed in the present clinical study indicated its utility in TYPEII DM management. In present clinical study significant improvement was observed in blood pressure control, Weight reduction and BMI of Type-II DM patients after three consecutive follow-ups of dietary interventions and life style modification. The clinical data showsthatbeforelife style modifications, 44.4% patientshavenormal systolic blood pressure, 33.3% were having raised systolic blood pressure in the range of 130-150 mm/Hg, and 22.2% patients are belonged to hypertensive group in the range of 150-190 After dietary interventions and life style modifications, above data was changed to 65.5% 26.6%, and 7.7% respectively. The data of present clinical study indicated that before life style modifications, 41.1% patients are having normal diastolic blood pressure, 46.6% patients were having had raised diastolic blood pressure in the range of 80-90 mm/Hg.12.2% patients had raised to hypertensive group in the range of 90-100 mm/Hg. No patients in this study have reported diastolic blood pressure above 100 mm/Hg [23].

LIFE-STYLE MODIFICATIONS

Details of life style modifications advised to the patient are as follows:

Early morning awakening, Brisk walking/light exercises for 30 min, Massage/swimming, Yoga, After lunch walking for 15 min and finally after dinner slow

walking for 15 min. Patients were advised to sleep only 6-7 h during the night and avoid sleep during day time. Patients were totally prohibited to take sweet items, fried items, fast foods, meat, milk products, cold drinks, chocolates, alcohol substances, dry fruits, curd, pickles, potato, sweet-potato, bread, butter, fermented items, etc. The assessment was done with symptoms of type II Diabetes mellitus polyuria, polyphagia, polydipsia, weakness, always desire to occupy bed, blurring vision.

In a study parameters as assessed on blood pressure, body weight, BMI, plasma glucose (FPG); 2-h plasma glucose (2-hPG) [24].

CONCLUSION

Based on published literature study it can be concluded that life style modifications and dietary interventions are two important tools by which adequate glycaemic control can be obtained in previously diagnosed type-2 DM patients. Thus these tools are useful in patients, who are on anti-diabetic medication, without proper control on glycemic index. Emphasize on patient counseling the patient should be instructed discontinue drugs immediately and report unexplained hyperventilation, myalgia, malaise, unusual somnolence or other nonspecific symptoms of early lactic acidosis. Warn to patients not to consume excessive amounts of alcohol while taking metformin. Instruct to patient not to change drug dosage without medical approval. Encourage to patient to report abnormal blood glucose levels and advise to patient no to take medications including over the counter (OTC), without medical approval [25].

REFERENCES

- 1. Mohan V, Sandeep S, Deepa R, Shah B, Varghese C, *et al.* Epidemiology of type 2 Diabetes: Indian scenario. *Indian J Med Res*, 125, 2007, 217-30.
- 2. Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with life-style intervention or metformin. *N Engl J Med*, 346, 2002, 393-403.
- 3. Collier CA, Bruce CR, Smith AC, Lopaschuk G, Dyck DJ, *et al.* Metformin counters the insulin-induced suppression of fatty acid oxidation and stimulation of triacylglycerol storage in rodents' skeletal muscle. *Am J Physiol Endocrinal Metab*, 219(1), 2006, 182-189.
- 4. Kim YD, Park KG, Lee YS, Park YY, Kim DK, Nedumaran B, *et al.* Metformin inhibits hepatic gluconeogenesis through AMP-activated protein kinase-dependent regulation of the orphan nuclear receptor SHP. *Diabetes*, 57(2), 2008, 306-314.
- 5. Shorr RI, Ray WA, Daugherty JR, Griffin MR. Individual sulfonylureas and serious hypoglycemia in older people. *J Am Geriatr Soc*, 44(7), 1996. 751-755.
- Van Staa T, Abenhaim L, Monette J. Rates of hypoglycaemia in users of sulfonylureas. J Clin Epidemiol. 50(6), 1997, 735-741.
- 7. Scheen AJ. Drug interactions of clinical importance with antihyperglycaemic agents: an update. *Drug Safi*, 28(7), 2005, 601-631.
- 8. Chiniwala N, Jabbour S. Management of diabetes mellitus in the elderly. *Curr Opin Endocrinal Diabetes Obese*, 18(2), 2011, 148-152.
- 9. Fuhlendorff J, Rorsman P, Kofod H, Brand CL, Rolin B, MacKay P, *et al.* Stimulation of insulin release by repaglinide and glibenclamide involves both common and distinct processes. *Diabetes*, 47(3), 1998. 345-351.
- 10. Yki-Jarvinen H. Thiazolidinediones. N Engl J Med, 351(11), 2004, 1106-1118.
- 11. Yoon KH, Lee JH, Kim JW, Cho JH, Choi YH, Ko SH, et al. Epidemic obesity and type 2 diabetes in Asia. Lancet, 368(9548), 2006, 1681-1688.

- 12. Coniff RF, Shapiro JA, Seaton TB, Bray GA. Multicentre, placebo-controlled trial comparing acarbose (BAY g 5421) with placebo, tolbutamide, and tolbutamide-plus-acarbose in non-insulin-dependent diabetes mellitus. *Am J Med*, 98(5), 1995, 443-451.
- 13. Kawamori R, Tajima N, Iwamoto Y, Kashiwagi A, Shimamoto K, Kaku K, *et al.* Voglibose Ph-3 Study GroupVoglibose for prevention of type 2 diabetes mellitus: a randomized, double-blind trial in Japanese individuals with impaired glucose tolerance. *Lancet*. 373(9675), 2009, 1607-1614.
- 14. Stonehouse AH, Darsow T, Maggs DG. Incretin-based therapies. J Diabetes, 4(1), 2012, 55-67.
- 15. Pratley RE, Salsali A. Inhibition of DPP-4: a new therapeutic approach for the treatment of type 2 diabetes. *Curr Med Res Opin*, 23(4), 2007, 919-931.
- 16. Barnett A. DPP-4 inhibitors and their potential role in the management of type 2 diabetes. *Int J Clin Pract*, 60(11), 2006, 1454-1470.
- 17. Mayfield JA, White RD. Insulin therapy for type 2 diabetes: rescue, augmentation, and replacement of beta-cell function. *Am Fam Physician*, 70(3), 2004, 489-500.
- 18. Burge MR, Schade DS. Insulins. Endocrinol Metab Clin North Am, 26(3), 1997, 575-598
- 19. Cameron CG, Bennett HA. Cost-effectiveness of insulin analogues for diabetes mellitus. CMAJ, 180(4), 2009, 400-407.
- 20. Rosenstock J, Lorber DL, Gnudi L, Howard CP, Bilheimer DW, Chang PC, *et al.* Prandial inhaled insulin plus basal insulin glargine versus twice daily biaspart insulin for type 2 diabetes: a multicenterrandomized trial. Lancet, 375(9733), 2010, 2244-2253.
- 21. Mikhail N. Quick-release Bromocriptine for Treatment of Type 2 diabetes. Curr Drug Deliv, 8(5) 2011, 511-6.
- 22. Tahrani AA, Bailey CJ, Del Prato S, Barnett AH. Management of type 2 diabetes: new and future developments in treatment. *Lancet*, 378(9786), 2011, 182-197.
- 23. Boffetta P, Mclerran D, Chan Y, Manami I, Sinha R, Gupta PC, et al. Body mass index and diabetes mellitus in Asia. A cross sectional pooled analysis of 900,000 individuals in the Asia cohort consortium, *PLoS One*, 6(6), 2011, 19930.
- 24. Blickle JF. Meglitinide analogues: a review of clinical data focused on recent trials. Diabetes Metab, 32(2), 2006, 113-120.
- 25. Black C, Cummins E, Royle P, Philip S, Waugh N. The clinical effectiveness and cost-effectiveness of inhaled insulin in diabetes mellitus: a systematic review and economic evaluation. *Health Technol Assess*, 11(33), 2007, 1-126.