International Journal of Multidisciplinary and Current Research ISSN: 2321-3124
Research Article Available at: http://ijmcr.com

Prescribing Pattern and Glycemic Control of type 2 Diabetes Mellitus

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Accepted 25 Nov 2016, Available online 27 Nov 2016, Vol.4 (Nov/Dec 2016 issue)

Abstract

A cross sectional descriptive study was carried out in order to assess the prescription pattern of oral anti diabetic drugs and glycemic control of type 2 diabetic patients in rural area. This study was performed among 38 diabetic patients who randomly visited Elgabrab Medical Center. In this study age of the patients was 55.44 ±15.53 years. There were 12 (31.6 %) male patients and 26 (68.4%) female patients. The weight of the patients was 67.4 ± 10.4 kilogram. The study resulted that (65.78 %) of patients who visited the centre had poor glycemic control.

Keywords: *Glycemic Control, Type 2 Diabetes, Prescribing Pattern, Elgabrab, Diabetic Patient, Blood Glucose, Blood Pressure, Anti- diabetic Agent, Age, Gender, treatment.*

Introduction

Diabetes mellitus

Diabetes mellitus, often simply referred to as diabetes, is a group of metabolic diseases in which a person has high blood sugar, either because the body does not produce enough insulin, or because cells do not respond to the insulin that is produced(Lambert *et al.*, 2002).This high blood sugar produces the classical symptoms of polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (increased hunger).

The three main types of diabetes mellitus (DM) are

- Type 1 DM results from the body's failure to produce insulin, and presently requires the person to inject insulin. (Also referred to as insulin-dependent diabetes mellitus (IDDM) or "juvenile" diabetes)
- Type 2 DM results from insulin resistance, a condition in which cells fail to use insulin properly, sometimes combined with an absolute insulin deficiency. (Formerly referred to as noninsulin-dependent diabetes mellitus (NIDDM) or "adult-onset" diabetes)
- Gestational diabetes is when pregnant women, who have never had diabetes before, have a high blood glucose level during pregnancy. It may precede development of type 2 DM.

Other forms of diabetes mellitus include congenital diabetes, which is due to genetic defects of insulin secretion, cystic fibrosis-related diabetes, steroid diabetes induced by high doses of glucocorticoids, and several forms of monogenic diabetes. All forms of diabetes have been treatable since insulin became available in 1921, and type 2 diabetes may be controlled with medications. Both types 1 and 2 are chronic conditions that usually cannot be cured. Pancreas transplants have been tried with limited success in type 1 DM; gastric bypass surgery has been successful in many with morbid obesity and type 2 DM. Gestational diabetes usually resolves after delivery. Diabetes without proper treatments can cause many complications. Acute complications includehypoglycemia, diabetic ketoacidosis, or non ketotic hyperosmolar coma. Serious long-term complications include diseasechronic renal failure, and diabetic retinopathy (retinal damage). Adequate treatment of diabetes is thus important, as well as blood pressure control and lifestyle factors such as smoking cessation and maintaining a healthy body weight.

Globally as of 2010, an estimated 285 million people have type 2 diabetes, making up about 90% of all diabetes cases(Association, 2010).

Comparison between type 1 and type 2:

Diabetes mellitus is classified into four broad categories: type 1, type 2, gestational diabetes and "other specific types". The "other specific types" are a collection of a few dozen individual causes The term "diabetes", without qualification, usually refers to diabetes mellitus. The rare disease diabetes insipidus similar symptoms as diabetes mellitus, but without disturbances in the sugar metabolism (*insipidus* means "without taste" in Latin).The

term "type 1 diabetes" has replaced several former terms, including childhood-onset diabetes, juvenile diabetes, and insulin-dependent diabetes mellitus (IDDM). Likewise, the term "type 2 diabetes" has replaced several former terms, including adult-onset diabetes, obesity-related diabetes, and noninsulin-dependent diabetes mellitus (NIDDM). Beyond these two types, there is no agreed-upon standard nomenclature. Various sources have defined "type 3 diabetes" as: gestational diabetes insulin-resistant type 1 diabetes (or "double diabetes"), type 2 diabetes which has progressed to require injected insulin, and latent autoimmune diabetes of adults (or LADA or "type 1.5" diabetes).

Types of diabetes

Type 1 diabetes

Type 1 diabetes mellitus is characterized by loss of the insulin-producing beta cells of the islets of Langerhansin the pancreas, leading to insulin deficiency. This type can be further classified as immune-mediated or idiopathic. The majority of type 1 diabetes is of the immune-mediated nature, where beta cell loss is a T-cell-mediated autoimmuneattack. There is no known preventive measure against type 1 diabetes, which causes approximately 10% of DM cases in North America and Europe. Most affected people are otherwise healthy and of a healthy weight when onset occurs. Sensitivity and responsiveness to insulin are usually normal, especially in the early stages. Type 1 diabetes can affect children or adults, but was traditionally termed "juvenile diabetes" because a majority of these diabetes cases were in children.

"Brittle" diabetes, also known as unstable diabetes or labile diabetes is a term that was traditionally used to describe to dramatic and recurrent swings in glucose levels, often occurring for no apparent reason in insulin-dependent diabetes. This term, however, has no biologic basis and should not be used(Lawrence *et al* 2008). There are many different reasons for type 1 diabetes to be accompanied by irregular and unpredictable hyperglycemias, frequently with ketosis, and sometimes serious hypoglycemias, including an impaired counter regulatory response to hypoglycemia, occult infection, gastroparesis (which leads to erratic absorption of dietary carbohydrates), and endocrinopathies (e.g., Addison's disease) (Lawrence *et al.*, 2008) .These phenomena are believed to occur no more frequently than in 1% to 2% of persons with type 1 diabetes(Rodbard *et al.*, 2009).

Type 2 diabetes

Type 2 diabetes mellitus is characterized by insulin resistance, which may be combined with relatively reduced insulin secretion .The defective responsiveness of body tissues to insulin is believed to involve the insulin receptor. However, the specific defects are not known. Diabetes mellitus cases due to a known defect are classified separately. Type 2 diabetes is the most common type. In the early stage of type 2, the predominant abnormality is reduced insulin sensitivity. At this stage, hyperglycemia can be reversed by a variety of measures and medications that improve insulin sensitivity or reduce glucose production by the liver(Lambert *et al*., 2002).

Gestational diabetes

Gestational diabetes mellitus (GDM) resembles type 2 diabetes in several respects, involving a combination of relatively inadequate insulin secretion and responsiveness. It occurs in about 2%–5% of all pregnancies and may improve or disappear after delivery. Gestational diabetes is fully treatable, but requires careful medical supervision throughout the pregnancy. About 20%–50% of affected women develop type 2 diabetes later in life. Though it may be transient, untreated gestational diabetes can damage the health of the fetus or mother. Risks to the baby include macrosomia (high birth weight), congenital cardiac and central nervous system anomalies, and skeletal muscle malformations. Increased fetal insulin may inhibit fetal surfactant production and cause respiratory distress syndrome. Hyperbilirubinemia may result from red blood cell destruction. In severe cases, perinatal death may occur, most commonly as a result of poor placental perfusion due to vascular impairment. Labor induction may be indicated with decreased placental function. A Caesarean section may be performed if there is marked fetal distress or an increased risk of injury associated with macrosomia, such as shoulder dystocia. A 2008 study completed in the U.S. found the number of American women entering pregnancy with pre-existing diabetes is increasing. In fact, the rate of diabetes in expectant mothers has more than doubled in the past six years(Blueprint).This is particularly problematic as diabetes raises the risk of complications during pregnancy, as well as increasing the potential for the children of diabetic mothers to become diabetic in the future.

Other types

Pre diabetes indicates a condition that occurs when a person's blood glucose levels are higher than normal but not high enough for a diagnosis of type 2 DM. Many people destined to develop type 2 DM spend many years in a state of pre diabetes which has been termed "America's largest healthcare epidemic(Cooke *et al.*, 2008). Latent autoimmune diabetes of adults (LADA) is a condition in which type 1 DM develops in adults. Adults with LADA are frequently initially misdiagnosed as having type 2 DM, based on age rather thanetiology.Some cases of diabetes are caused by the body's tissue receptors not responding to insulin (even when insulin levels are normal, which is what separates it from type 2 diabetes); this form is very uncommon. Genetic mutations

(autosomal or mitochondrial) can lead to defects in beta cell function. Abnormal insulin action may also have been genetically determined in some cases. Any disease that causes extensive damage to the pancreas may lead to diabetes (for example, chronic pancreatitis and cystic fibrosis). Diseases associated with excessive secretion of insulin-antagonistic hormones can cause diabetes (which is typically resolved once the hormone excess is removed). Many drugs impair insulin secretion and some toxins damage pancreatic beta cells. The ICD-10 (1992) diagnostic entity, *malnutrition-related diabetes mellitus* (MRDM or MMDM, ICD-10 code E12), was deprecated by the World Health Organization when the current taxonomy was introduced in 1999(Boussageon *et al.*, 2011).

Signs and symptoms

The classical symptoms of diabetes are polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (increased hunger). Symptoms may develop rapidly (weeks or months) in type 1 diabetes, while they usually develop much more slowly and may be subtle or absent in type 2 diabetes.

Prolonged high blood glucose can cause glucose absorption in the lens of the eye, which leads to changes in its shape, resulting in vision changes. Blurred vision is a common complaint leading to a diabetes diagnosis; type 1 should always be suspected in cases of rapid vision change, whereas with type 2 change is generally more gradual, but should still be suspected. A number of skin rashes which can occur in diabetes are collectively known as diabetic dermadromes(Risérus *et al.*, 2009).

Diabetic emergencies

People (usually with type 1 diabetes) may also present with diabetic ketoacidosis, a state of metabolic deregulation characterized by the smell of acetone, a rapid, deep breathing known as Kussmaul breathing, nausea, vomiting and abdominal pain, and altered states of consciousness. A rare but equally severe possibility is hyperosmolar non ketotic state, which is more common in type 2 diabetes and is mainly the result of dehydration.

Complications:

All forms of diabetes increase the risk of long-term complications. These typically develop after many years (10–20), but may be the first symptom in those who have otherwise not received a diagnosis before that time. The major long-term complications relate to damage to blood vessels. Diabetes doubles the risk of cardiovascular disease(Shivashankar *et al.*, 2011).The main "macro vascular" diseases (related to atherosclerosis of larger arteries) are ischemic heart disease (angina and myocardial infarction), stroke and peripheral vascular disease. Diabetes also causes "micro vascular" complications damage to the small blood vessels(Sattar *et al.*, 2010).Diabetic retinopathy, which affects blood vessel formation in the retina of the eye, can lead to visual symptoms, reduced vision, and potentially blindness. Diabetic nephropathy, the impact of diabetes on the kidneys, can lead to scarring changes in the kidney tissue, loss of small or progressively larger amounts of protein in the urine, and eventually chronic kidney disease requiring dialysis. Diabetic neuropathy is the impact of diabetes on the nervous system, most commonly causing numbness, tingling and pain in the feet and also increasing the risk of skin damage due to altered sensation. Together with vascular disease in the legs, neuropathy contributes to the risk of diabetes-related foot problems (such as diabetic foot ulcers) that can be difficult to treat and occasionally require amputation.

Causes

The cause of diabetes depends on the type.

Type 1 diabetes is partly inherited, and then triggered by certain infections, with some evidence pointing at Coxsackie B4 virus. A genetic element in individual susceptibility to some of these triggers has been traced to particular HLA genotypes (i.e., the genetic "self" identifiers relied upon by the immune system). However, even in those who have inherited the susceptibility, type 1 DM seems to require an environmental trigger. Type 2 diabetes is due primarily to lifestyle factors and genetics(Organization, 2013)

Pathophysiology

The fluctuation of blood sugar (red) and the sugar-lowering hormone insulin (blue) in humans during the course of a day with three meals - one of the effects of a sugar-rich a starch-rich meal is highlighted.

Mechanism of insulin release in normal pancreatic beta cells - insulin production is more or less constant within the beta cells. Its release is triggered by food, chiefly food containing absorbable glucose. Insulin is the principal hormone that regulates uptake of glucose from the blood into most cells (primarily muscle and fat cells, but not central nervous system cells). Therefore, deficiency of insulin or the insensitivity of its receptors plays a central role in all forms of diabetes mellitus. Humans are capable of digesting some carbohydrates, in particular those most common in food; starch, and some disaccharides such as sucrose, are converted within a few hours to simpler forms, most notably the monosaccharideglucose, the principal carbohydrate energy source used by the body. The rest are passed on for processing by gut flora largely in the colon. Insulin is released into the blood by beta cells (β-cells), found in the islets of Langerhans in the pancreas, in response to rising levels of blood glucose, typically after eating. Insulin is

used by about two-thirds of the body's cells to absorb glucose from the blood for use as fuel, for conversion to other needed molecules, or for storage. Insulin is also the principal control signal for conversion of glucose to glycogen for internal storage in liver and muscle cells. Lowered glucose levels result both in the reduced release of insulin from the β-cells and in the reverse conversion of glycogen to glucose when glucose levels fall. This is mainly controlled by the hormone glucagon, which acts in the opposite manner to insulin. Glucose thus forcibly produced from internal liver cell stores (as glycogen) re-enters the bloodstream; muscle cells lack the necessary export mechanism. Normally, liver cells do this when the level of insulin is low (which normally correlates with low levels of blood glucose).

Higher insulin levels increase some anabolic ("building up") processes, such as cell growth and duplication, protein synthesis, and fat storage. Insulin (or its lack) is the principal signal in converting many of the bidirectional processes of metabolism from a catabolic to an anabolic direction, and *vice versa*. In particular, a low insulin level is the trigger for entering or leaving ketosis (the fat-burning metabolic phase).

If the amount of insulin available is insufficient, if cells respond poorly to the effects of insulin (insulin insensitivity or resistance), or if the insulin itself is defective, then glucose will not have its usual effect, so it will not be absorbed properly by those body cells that require it, nor will it be stored appropriately in the liver and muscles. The net effect is persistent high levels of blood glucose, poor protein synthesis, and other metabolic derangements, such as acidosis.

When the glucose concentration in the blood is raised beyond its renal threshold (about 10 mmol/L, although this may be altered in certain conditions, such as pregnancy), reabsorption of glucose in the proximal renal tubule is incomplete, and part of the glucose remains in the urine (glycosuria). This increases the osmotic pressure of the urine and inhibits reabsorption of water by the kidney, resulting in increased urine production (polyuria) and increased fluid loss. Lost blood volume will be replaced somatically from water held in body cells and other body compartments, causing dehydration and increased thirst.

Diagnosis

Diabetes mellitus is characterized by recurrent or persistent hyperglycemia, and is diagnosed by demonstrating any one of the following(Boussageon *et al.*, 2011).

- Fasting plasma glucose level ≥ 7.0 mmol/l (126 mg/dl)
- Plasma glucose ≥ 11.1 mmol/l (200 mg/dL) two hours after a 75 g oral glucose load as in a glucose tolerance test
- Symptoms of hyperglycemia and casual plasma glucose ≥ 11.1 mmol/l (200 mg/dl)
- Glycated hemoglobin (Hb A1C) ≥ 6.5%(Selvin *et al.*, 2010).

A positive result, in the absence of unequivocal hyperglycemia, should be confirmed by a repeat of any of the above methods on a different day. It is preferable to measure a fasting glucose level because of the ease of measurement and the considerable time commitment of formal glucose tolerance testing, which takes two hours to complete and offers no prognostic advantage over the fasting test(Control *et al.*, 2005). According to the current definition, two fasting glucose measurements above 126 mg/dl (7.0 mmol/l)are considered diagnostic for diabetes mellitus.

People with fasting glucose levels from 100 to 125 mg/dl (5.6 to 6.9 mmol/l) are considered to have impaired fasting glucose. Patients with plasma glucose at or above 140 mg/dL (7.8 mmol/L), but not over 200 mg/dL (11.1 mmol/L), two hours after a 75 g oral glucose load are considered to have impaired glucose tolerance. Of these two pre diabetic states, the latter in particular is a major risk factor for progression to full-blown diabetes mellitus, as well as cardiovascular disease. Glycated hemoglobin is better than fasting glucose for determining risks of cardiovascular disease and death from any cause(Charles *et al.*, 1997).

Management

Diabetes mellitus is a chronic disease which cannot be cured except in very specific situations. Management concentrates on keeping blood sugar levels as close to normal ("euglycemia") as possible, without causing hypoglycemia. This can usually be accomplished with diet, exercise, and use of appropriate medications (insulin in the case of type 1 diabetes, oral medications, as well as possibly insulin, in type 2 diabetes).

Patient education, understanding, and participation is vital, since the complications of diabetes are far less common and less severe in people who have well-managed blood sugar levels.(Adler *et al*. 2000) The goal of treatment is an HbA1C level of 6.5%, but should not be lower than that, and may be set higher. Attention is also paid to other health problems that may accelerate the deleterious effects of diabetes. These include smoking, elevated cholesterol levels, obesity, high blood pressure, and lack of regular exercise(Pignone *et al.*, 2011).

Lifestyle

There are roles for patient education, dietetic support, sensible exercise, with the goal of keeping both short-term and long-term blood glucose levels within acceptable bounds. In addition, given the associated higher risks of cardiovascular disease, lifestyle modifications are recommended to control blood pressure(Polisena *et al.*, 2009).

Medications

Insulin therapy

Type 1 diabetes is typically treated with a combinations of regular and NPH insulin, or synthetic insulin analogs. When insulin is used in type 2 diabetes, a long-acting formulation is usually added initially, while continuing oral medications. Doses of insulin are then increased to effect(Wild *et al.*, 2004).

Types of insulin

Soluble insulins

These were first introduced in 1922. They have a rapid onset of action (within 15-30 minutes) and a relatively short overall duration of action of six to eight hours. They play an important part in both daily maintenance of diabetic patient subcutaneous injection, and also in managing emergencies when they can be given intravenously or intramuscularly.

Other insulin preparations are not suitable for intravenous orintramuscular use.

New recombinant insulin analogues

These have a very rapid onset and very short action, and have been developed altering the structure and thus the property of the insulin. The preparations available in the United Kingdom at present are Insulin Lispro (Humalog) and Insulin As part (Novo Rapid). They have some advantages because they may be given immediately before meals (or even immediately after meals if necessary). By virtue of their very short action, there is Lesshypoglycemia before the next meal, and when they are used before the main evening meal nocturnal hypoglycemia iseffectively reduced. There is a risk of postprandial hypoglycemia if they are used before a meal with a very high fat content because of the delayed gastric emptying. Duration of action is short and does not normally exceed three hours, and their use is therefore inappropriate if the gap between meals exceeds about four hours. Pre-prandial blood glucose levels are slightly higher than with conventional soluble insulins. They are also ideal for use in continuous subcutaneous insulin infusion pumps (CSII).

Protamine insulins

These are medium duration insulins introduced in Denmark during the 1930s. Isophane insulin is the most frequently used insulin in this group. Insulin zinc suspensions these were first introduced during the 1950s; there are several preparations with widely ranging durations of action. There are limited indications for using insulins with a very long duration of action.

Insulin glargine

This is a new prolonged action, soluble insulin analogue (clear solution) forming a micro precipitates after subcutaneous injection. Its onset of action is after about 90 minutes, it has a prolonged plateau rather than a peak, and lasts 24 hours or more. Thus it mimics more closely the basal insulin secretion of healthy people. When taken at bedtime it reduces the incidence of nocturnal hypoglycemia, and also reduces the pre-breakfast hyperglycemia. It does not appear to reduce symptomatic or severe hypoglycemia during the day, and there is no significant beneficial effect on overall diabetic control. More extensive clinical experience in using this insulin is still needed.

Insulin mixtures

Some preparations of insulin are presented as proprietary mixtures in either vials or pen cartridges, eliminating the need for patients to mix insulins in the syringe. The most popular mixture contains 30% soluble insulin and 70% isophane, whereas the whole range also includes ratios 10%/90%,20%/80%, 40%/60%, and 50%/50%. These insulin mixtures represent a considerable advantage for many patients, especially those who find it difficult to mix insulins in the syringe or those whose visual acuity is impaired.

Oral antidiabetic agents

Metformin is generally recommended as a first line treatment for type 2 diabetesas there is good evidence that it decreases mortality. Routine use of aspirin, however, has not been found to improve outcomes in rashes and jaundice. Only one sulphonylurea should be uncomplicated diabetes.

- Sulphonylureas stimulate insulin secretion
- Meglitidine analogues stimulate insulin secretion
- Biguanides (metformin) reduce hepatic gluconeogenesis and enhance glucose uptake.
- Thiazolidinedione enhance insulin sensitivity.
- α_ glucosidase inhibitors (acarbose) reduce absorption of complex carbohydrates.
- Pharmacological agents to assist weight reduction:
- Antihypertensive and lipid lowering agents

Sulphonylureas

Seven sulphonylureas are available. They are remarkably safe and free from side effects, although rare toxic effects have been reported, including used at a time since there is nothing to be gained from any combination of these drugs and there is no evidence that any one drug is likely to be more successful than another.

Selecting a sulphonylurea is largely a matter of personal choice, though it is now usual to use one of the shorter acting, metabolized drugs such as gliclazide or glipizide, which are suitable for all ages and for those with renal impairment as well, Glibenclamide, which has the advantage of once-daily use. Is still suitable for younger patients, but is contraindicated in the elderly. Glimepiride

is also given once daily and may cause lesshypoglycemia. Excessive doses can cause hazardous (even fatal) hypoglycemia, and it is thus usual to start treatment with the smallest useful dose. If hypoglycemia does occur in a patient taking a sulphonylurea, the drug should be stopped orat the very least the dose substantially reduced.

Chlorpropamide is now obsolete. It has a very long half life,thus increasing the risk of hypoglycemia, and many patients experience an unpleasant facial flush on drinking very small amounts of alcohol.

Meglitidine analogue

The mode of action of this group of drugs is similar to that of sulphonylureas though acting at a different site. Their Advantages are the rapid onset and short half life, efficacy when taken just 15 minutes before meals, and duration of effect ofno more than three hours. They are omitted if no meal is taken.

There may be some benefit in reducing postprandial glycaemia and in theory at least there might be less hypoglycemia.

Nateglinide is one of a new class of oral hypoglycemic agents, namely an amino acid derivative. Insulin release after meals is both faster and of shorter duration than that with either sulphonylureas or repaglinide, giving less postprandialhyper-insulinaemia and less reactive hypoglycemia. It is licensedonly for use in combination with metformin, but not formonotherapy or substitution for conventional sulphonylureas.

Biguanides: metformin

Biguanides act chiefly by reducing hepatic glucose production. They also enhance peripheral glucose uptake, and to some extent reduces carbohydrate absorption. Metformin is the only biguanide available in the United Kingdom. It is the drug of(Boussageon *et al.*, 2011)choice in the treatment of overweight Type 2 diabetic patients when di*et al*one has failed. UKPDS found some evidence for a reduction in mortality after the use of metformin.

Lactic acidosis is a serious consequence of the inappropriate use of metformin. It is contraindicated in any patient with renal failure, and serum creatinine should be monitored. A creatinine concentration above 150_mol/l indicates that the drug should be stopped. Metformin should not be used in any seriously ill or shocked patient, nor in those with heart failure, serious liver disease or a very high alcohol intake. It is not appropriate for the treatment of thin diabetic patients nor for use in frail elderly patients.

α-Glucosidase inhibitors

These agents block the enzyme responsible for the breakdown of complex carbohydrates in the gut and can effectively reduce the increase in blood glucose after a meal. Acarbose acts in this way and can be used alone or in combination with other oralhypoglycemic agents. Its hypoglycemic effect is relatively small and the severe flatulence which develops (to some extent avoidable by starting with small amounts) deters many patients from using it.

Thiazolidinedione

This newly introduced group of hypoglycemic agents acts byreducing insulin resistance and by activation of the peroxisomeproliferator activated receptor _ expressed predominantly in a dipose tissue.

These drugs are licensed for use with metformin if this alone has failed to control the diabetes, or with a sulphonylurea if metformin is either not tolerated or contraindicated (for example, in renal failure). In the European Union they are not licensed for use alone or in combination with insulin, andshould not be given to patients with a history of he art failure, or during pregnancy. They may cause edema, a minorreduction of haemoglobin, and a small increase of HDLcholesterol. There are very rare reports of liver dysfunction, and liver function should be monitored before, and every two months after, starting treatment, for the following 12 months.

Drugs for management of obesity

There is a limited place for the use of medication in assisting with weight reduction in the obese diabetic patient. The use ofsuch drugs is restricted to those whose BMI is 28 or more and who are between the ages of 18 and 65 years; they should onlybe prescribed for individuals who have lost at least 2·5 kg bodyweight by diet and exercise during the preceding month.

Patients should continue to be supported by their advisers and counselors throughout treatment. Orlistat inhibits fat absorption by inhibition of pancreatic lipase. Weight reduction indicating a successful response should be greater than 5%after 12 weeks, in which event prescription may be continued for one year to a limit of two years, otherwise treatment should cease. Unpleasant oily leakage and steatorrhoea can occur. Sibutramine also acts centrally as a serotonin and noradrenaline reuptake inhibitor and enhances the satiety response. It is used as an adjunct to weight maintenance after weight loss. Full details of its use and contraindications are to be found in the *BNF*.

Indications for insulin in Type 2 diabetes

Approximately 6% of non-obese and 2% of obese Type 2diabetic patients need to start insulin each year. Predicting the need for insulin is difficult: those of lean body mass, especially in the presence of islet cell antibodies, are at greatest risk. Whether to give insulin to Type 2 diabetic patients is one of the most important yet difficult decisions to be made in treating these patients.

Failure to give insulin to some patients results in protracted and needless malaise if not actual danger.

On the other hand, giving insulin inappropriately can cause needless problems, notably from hypoglycemia and weight gain.

Indications for giving insulin to Type 2 diabetic patients who are inadequately controlled despite adherence to their recommended diet and or hypoglycemic agents are as follows:

• Continuing weight loss (even if this is insidious), and persistent symptoms or both. Insulin treatment in these patients almost always results in a substantial improvement in health.

• A non-obese patient without symptoms whose weight is stable and who is conscientious with existing medication. Diabetic control will usually improve, and about half of the patients will enjoy an improvement in well-being.

• An obese patient without symptoms whose weight is stable presents an even more difficult problem. The correct management is to ensure that they are taking their medication, together with intensification of diet, but sometimes insulin may be needed simply to improve control of diabetes in order to reduce long-term complications during the following decade or more.

A reduction of HbA1C of approximately 2% together with weight gain of around 5-7 kg can be expected. Unfortunately improvement in glycaemic control is not always achieved. Patient choice is important here, and some prefer not to take insulin after all explanations have been presented. Reluctant patients can be given a three-month trial of insulin and then make their decision, which experience shows to be usually affirmative.

Those with a short life expectancy do not necessarily benefit, and those with other medical disorders will require individual consideration.

• Insulin is often required in patients with undercurrent illness. Many disorders, notably infections, increase insulin resistance leading to the temporary need for insulin. Withdrawal of insulin after recovering from the illness is important provided adequate control is achieved and maintained.

Corticosteroids always exacerbate hyperglycaemia and often precipitate the need for insulin. This should not deter doctor from prescribing them when they are needed.

Combination treatment with insulin and metformin

Metformin can be given together with insulin to overweight Type 2 diabetic patients: this can to a small extent limit the inevitable weight gain following introduction of insulin. A combination of sulphonylureas with insulin gives little benefit and has the added disadvantage that patients must continue with both modes of treatment (Peter).

Method

Study type

This was prospective cross-sectional descriptive survey.

Study site

This study was performed in Elgabrab village in River Nile State in the North Sudan.

Study design

This study was performed to assess prescribing pattern of ant diabetic agent and glycemic control in type 2 diabetes in rural area.

Source of data

All necessary and relevant information were collected from Prescriptions, and verbal communications with patients.

Collection of data

The questionnaire was prepared and approved by department of clinical pharmacy of Omdurman Islamic university, questionnaire paper was composed of the patient information as well as medication information of age, gender, weight, height, family history, medical history, chronic disorders, acute disorder, treatment, blood pressure and random blood glucose.

Inclusion criteria

Patients who included in the studytype 2 diabetic patient of any age group above 30 years.

Exclusion criteria

Patients who excluded from this survey were under 30 years.

Statistical data analysis

Statistical analysis of the data was performed using INSTAT Excel Sheet and SPSS program for windows with $p < 0.05$ considered significant

Result

The population

In 4 days 300 patients visited medical center in Elgabrab village, 38 were type 2 diabetic patients with males comprising 31.6% (n=12) and females 68.4% (n=26).

Age distribution

In study of the age distribution of the patients , it was found that the most age groups affected with type 2 DM were 30-50years 17 (44.7%) and 51-70years 17 (44.7%) then 71-90 years 3 (7.9%) and the least 91-100 1(2.6%) patient. as shown in the table-2 below:

Weights distribution

In study of the weight distribution we found ,1 (2.6%) patient with weight range of 40-50 kg, 11(28.9%)

patients had weight between 51-60 kg,16 (42.1%) patients weighing between 61-70kg, which is the most weight suffering from diabetes,5 (13.2%) patients weighing between 71-80 kg, 4 (10.5%) patients of weight between 81-90 kg, 1 (2.6%) patient weighing between 91-100 kg. as shown below by the table-3 :

The height distribution

Study of the heights distribution we found,1 (2.6%) patient of height between 140-150 cm, 16 (42.1%) patients with height between 151-160 cm which was the most height involved, 12 (31.6%) patient with height between 161-170 cm, 7 (18.4%) patient with height of 171-180 cm, 2 (5.3%) patient with height between 181-190 cm. As shown below in the table-4:

Family history

In study of patients family history, 9 (23.7%) patients had diabetes mellitus , and the same percentage of patients without family history of chronic disease ,4 (10.5 %) patients with hypertension , 10(26.3 %) patients with both diabetes and hypertension, 1 (2.6%) patient s with asthma and 5 (13.2) patients with other disease(acute disorders). As shown in the table-5 below:

Medical history

In study of the medical history we found, 16 (42.1%) patients with diabetes mellitus, 5 (13.2%) patients with other disorders, 17 (44.7%) patients with diabetes mellitus and other disorders. As shown by table-6 below:

Therapeutic agents

In the study of the therapeutic agents, 30 (78.9%) patients were treated by glibenclamide, 4 (10.5%) patients were treated by metformin and 4 (10.5%) patients were treated with combination of glibenclamide and metformin. As shown in the table-7 below:

Table (1): current anti hyperglycemic treatment of the patient

Treatment	No. of patients	Percent
Glibenclamide	30	78.9
Metformin	4	10.5
glibenclamide, metformin	4	10.5
Total	38	100.0

Blood pressure

In study of the blood pressure, 6 (15.8%) patients had BP 120/75- 128/85 mg Hg, 18 (47.4%) patients had BP 130/65-135/90 mg Hg, 9 (23.7%) patient with BP 140/80-145/90 mg Hg, 1 (2.6%) patient with BP 160/80-160/85 mg Hg, 4(10.5%) patient with BP 183\80-190/85 mg Hg. As shown by the table-8 below:

Glycemic control

In the study of glycaemic control we found, 13 (34.2%) patients had controlled blood glucose, 25 (65.8%) patient had uncontrolled blood glucose. As shown by the table(2).

Table (2): Glycemic control

Random blood glucose.	No. of patients	Percent
Controlled	13	34.2
Uncontrolled	25	65.8
Total	38	100.0

Treatment against gender

In study of 38 patients treatment vs. gender, 31 patients were treated by glibenclamide (8 male and 23 female) , 4 patients were treated by metformin (2 male and 2 female) and 3 patients were treated by combination of glibenclamide and metformin.P value was 0.44. As shown in the table (3).

Table (3): Treatment vs. gender

Treatment	Male	female	Total
Glibenclamide	8	23	31
Metformin	2	2	4
Glibenclamide, Metformin	2	1	3
Total	12	26	38

Treatment against age

In the study of the 38 patients treatment against age, we found among 31 patients treated with glibenclamide ,13 patients of age group 30-50 years, 14 patients of age group 51-70 years, 3 patient between 71-90 years, and 1 patient between 91 -100 as shown in the table (4).

Table (4): Treatment vs. age

Treatment	Age(Years)				Total
	30-50	51-70	71-90	91-100	
Glibenclamide	13	14	3	1	31
Metformin	4	0	0	0	4
Glibenclamide, Metformin	0	3	0	0	3
Total	17	17	3	1	38

Treatment against drug class

In the study of treatment against drug class of the 38 patient, 31 patients on sulfonylureas especially glibenclamide, 4 patients on biguanide (metformin), and 3 patients on combination of sulfonylureas plus biguanide (glibenclamide and metformin).P value was 0.97.

Treatment against random blood glucose

In the study of the treatment against random blood glucose, among the total 38 patients who treated with oral ant diabetic, 25 patients with uncontrolled blood glucose , and 13 patient with controlled blood glucose. Among the 25 patients with uncontrolled blood glucose, 21 patients were treated byglibenclamide, 1 patient was treated by metformin, and 3 patients were treated by combination of glibenclamide and metformin.

Among the 13 patients who had controlled blood glucose, 10 patients were treated by glibenclamide and 3 patients treated by metformin. P value was 0.97.

(Table 5): Treatment vs. random blood glucose

Treatment	Random Blood Glucose		Total
	No. of patient controlled	No. of patient uncontrolled	
Glibenclamide	10	21	31
Metformin	3	1	4
glibenclamide, metformin	0	3	3
Total	13(34.2%)	25 (65.8 %)	38

Discussions

Diabetes is a chronic disease requiring lifelong treatment. Although life style modification plays an important role in diabetes management, drugs become unavailable in many patients. This study analysed the prescription pattern and glycaemic control in type 2 diabetic patients attending medical centre in Elgabrab village.

In this study we found higher incidence of type 2 diabetes among young and elderly patients, with a high incidence in the age groups 30-50 and 51-70 years. In this study age of patients was 55.4 ± 15.5 years. A study from Netherlands reported an average age of 67 years(Naughton *et al.*, 1993).

Another study from Spain reported an average age of 60.5 ± 12.8 years(de Pablos-Velasco *et al.*, 2005). This study reported a lower age of patients compared to other studies.

In this study we found weight of patients was 67.4 ± 10.4 kilogram. Little glycaemic control was observed in weight groups 51-60 and 61-70 kilogram by 40% and 50%, respectively. Other weight groups show 100% failure in glycaemic control. Weight against glycaemic control was intermediate but not significant (p = 0.06).

In this study antidiabetic drugs accounted for (12.66%) of the total drugs prescribed. Among the antidiabetic, sulfonylureas accounted for (81.6%) of the total drugs, followed by biguanide (10.5%) and combination of them (7.9%). A study from Nepal reported biguanide (51.27%) as the most common drug class followed by sulfonylureas (35.35%)(Upadhyay *et al.*, 2007).Similar study from Taiwan reported sulfonylureas as the most common class followed by biguanides(Wei *et al.*, 2003).In this study (65.8%) of patient had poor glycaemiccontrol.A study from Mexico reported (45.6 %) of total patient had good glycaemic control and 54.4 % had poor glycaemic control. In this study glycaemic control showed failure rates of 70% (21 of 31 patients), 25% (1 of 4 patients) and 100% (3 of 3 patients) for glibenclamide, metformin, and glibenclamide plus metformin, respectively. In this study the Glycaemic control was not significantly affected by oral antidiabetic (P=0.97).

The choice of ant diabetic depends on the type of patients, their concurrent illness, cost factor, as well as availability of medicine, in general, glibenclamide associated with the risk of hypoglycaemia in elderly patients, and metformin require assessment of renal function.

Although metformin is the only proven oral ant diabetic that reduces morbidity, mortality and cardiovascular events however glibenclamide due availability and lower cost making it affordable for the patients in economically weak countries like Sudan.

Implications of this study

This study was the first of its kind in Elgabrab village to study the utilization pattern of ant diabetic drugs and glycaemic control.

Thus this study had provided a baseline data regarding the prescribing pattern in diabetes patients. This study had provided an open way for further research in this area.

Limitations

Our study had a few limitations. It was done for a short period of time and the number of patients studied was low. Hence similar studies covering large number of patients are required to confirm our findings.

Conclusion

Assessing prescription pattern of drugs for the relevance and adherence as per standard treatment guidelines is important for rational drug utilization which results in good management of the disease. Uncontrolled diabetes is a major health problem and is directly responsible for majority of cardio vascular events.

Despite of few positive adherences, the goal blood glucose was not attained in the study patients. Prescribers must be encouraged to adhere to the standard guidelines.

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