PharmacologyOnLine December 30, 2014

Archives • 2014 • vol.3 •106-111

TREATMENT PATTERN AND GLYCEMIC CONTROL OF ORAL HYPOGLYCAEMIC DRUGS AMONG TYPE II DM PATIENTS IN ERITREA

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Abstract

The present retrospective study aimed to explore the treatment pattern and glycemic control of oral antidiabetic drugs among type 2 diabetes mellitus patients in Asmara, Eritrea. This study was undertaken in the Diabetic Unit of Helibet Referral Hospital, Asmara. Two hundred case files were included in this study after they ran across the inclusion criteria of patients age of ≥ 20 years, who identified with type 2 diabetes and who underwent fasting plasma glucose (FPG) testing at least 3 times. The information collection was performed over the period of five months. The most usually prescribed anti-diabetic medications were sulfonylureas (Glibenclamide -131 and Glimipride - 60) and Metformin (74) either alone or in combination. Monotherapy was prescribed more (135, 67.5%) than combination therapy (65, 33.5%). No significant difference in FPG reduction was found among monotherapies. Whereas, in combination therapy Glibenclamide + Metformin combination was found to be more effective ($p = 0.01$). No treatment variations observed between current clinical practice and Eritrean National Treatment Guideline (Edition 2003) and Treatment Algarithm of International Diabetes Federation Eritrea (Africa region). On the other hand, just 37% prescriptions were adherent to American Diabetic Association's recommendation concerning Metformin as first-line monotherapy. In conclusion, Biquanides and sulphonyl ureas were prescribed and none other oral hypoglycemic drugs were ordered. Only, Multiple doses of basal Insulin have been prescribed for patients with inadequate glycemic control.

Key words: Eritrea, treatment practice, fasting plasma glucose, Glibenclamide, Glimipride and Metformin.

Introduction

Diabetes mellitus is the major burden up on health care in all countries [1]. According to the International Diabetes Federation (IDF) 366 million people had diabetes in 2011, by 2030 this will be risen to 552 million and 80% people with DM live in low and middle income countries [2]. The prevalence of diabetes is increasing rapidly in Sub Saharan Africa (SSA) like the rest of the world. It is estimated that over the next 20 years SSA will have the highest prevalence of DM of any region in the world [3]. A survey directed to investigate the burden of Non Communicable Diseases (NCDs) in Eritrea from 1998 to 2003 has shown that 2.3% of Eritrean had a prior diagnosis of DM and most likely the majority cases are undiagnosed, so it was judged that the actual prevalence of diabetes exceeded 5% [4, 5, 6]. Though the prevalence of DM in Eritrea is within low – medium category (0-7%), the increasing adult risk factors of DM both in males (8.3%) and females (9.2%) [7], poor treatment monitoring and low consciousness of the early symptoms of diabetes may shift this rate to high prevalence category (> 10%) with serious short and long term complications.

Many research works demonstrated that early diagnosis and effective treatment would control diabetes and its complications. Half a dozen different categories of OHG drugs approved to treat type II diabetes by the FDA, which include Sulphonyl ureas, Biguanides (Metformin), Alpha-glucosidaseinhibitors (eg, Acarbose), Thiazolidinediones (e.g., Rosiglitazone, Pioglitazone), Meglitinides (eg, Repaglinide, Nateglinide), and Dipeptidyl peptidase-4 inhibitors (eg, Sitagliptin, Saxagliptin). Nevertheless, all these drugs are not used as first line treatment because of their side effects and poor ability to improve other diabetic related outcome [8]. American Diabetic Association's (ADA) [9] updated statement endorse metformin as first course treatment. Nevertheless the widespread dissemination of national and international professional society recommendations current clinical practice is not known by many professionals and that make patients to experience irrational drug use. In addition to this issue diabetic patients experience deprived access to appropriate diabetes care in Sub-Saharan Africa because of inadequate health care systems, shortage of doctors and nurses with adequate training in diabetes, shortage or unaffordability of medication, and shortage of diagnostic tools and other equipments [3].

One of the least developed African countries, Eritrea is also confronting the problem of short supply of tablet medications and Insulin and even if they are available often unaffordable. And then it is a hard task for health care professionals to handle the disease effectively with the available medicines. Hence, this work is designed to explore the prescribing regimen and glycemic control of the prescribed drug. In addition, the present study aimed to determine the variations between the current treatment pattern with National and International guidelines. As far as we aware, this is the first study about a treatment pattern of type II DM in Eritrea and this too would help interested researchers to extend out further research in DM and to fulfill the literature gap that is present.

Methods

The present work was conducted in the Diabetic Unit of Helibet Referral Hospital, Asmara over the period of five months starting from Sep 2012 until January 13 and it was approved by the Medical Director of that Hospital. The case sheets were selected and included in this study after they met the inclusion standards. These were patients of age ≥ 20 years, identified with type 2 diabetes and underwent fasting plasma glucose (FPG) testing at least 3 times and no exclusion was made for patients with multiple diseases. So overall 200 complete case sheets were retrieved from patients' medical record room, Helibet referral hospital. A special patient data sheet was designed to collect the patients' demographic and treatment details such as age, sex, diagnosis, co-morbidities, Mean FPG, drug name, dosage form and dose. The blood glucose control was estimated by means of Fasting Plasma Glucose (FPG) which had been calculated at several levels: glucose level at the first visit was counted as a baseline, second visit as first-follow up and third visit as second-follow up.

Statistical analysis was performed using SPSS.18 version software. The average difference in the two groups was compared using student's t test, and three groups were compared using one way ANOVA, a *p*-value less than 0.05 was considered as significant. Data are shown as mean ± standard deviation and percentages.

Results

The study population consists of 97 males (48.5%) and 103 (51.5%) female patients (Table: 1). Sixty

percent of (120) patients were under 60 years of age and 80 patients (40%) were equal and above 60. The average age of the male and female patients was 57.16 ± 10. 204 and 55.91 ± 7.819 years, respectively. (Tab. 1).

Out of 200 patients, 49 (24.5%) patients were reported with hypertension as co-morbidity and all of them treated with ACEIs mainly Enalapril. One thirty five (67.5%) patients were prescribed with monotherapy and combination therapy was prescribed for 65 (22.5%) patients. Glibenclamide was prescribed more commonly than (131, 65.5 %) Metformin and Glimipride as monotherapy (74, 37%). Two types of two drug combinations were in practice which include Glimipride + Metformin and Glibenclamide + Metformin (Figure:1) and later one was prescribed more often (43, 21.5%). From the data collected, drugs were prescribed in the following order; Glibenclamide> Glibenclamide + Met>Glimipride>Glimipride + Met > Met.

Table: 2 shows the FPG reduction of various oral hypoglycemic drugs. A combination therapy had proven a significant FPG reduction (78.66±20.040, p=0. 02). There was no significant FPG reduction difference found among monotherapies. On the other hand, Glibenclamide + metformin combination was found to be more significant (58.672, *p= 0.01*) when comparison made with another combination.

The present study indicates that virtually all prescriptions were adherent to the ADA recommendation concerning the use of combination of metformin + sulphonyl urea and Metformin + Basal Insulin as second line two drug combination. Yet, just 4.5% (9 patients) prescriptions were adherent to ADA recommendation (2012) about metformin as first line monotherapy. Three drug combination is not in practice, but multiple insulin doses were prescribed with or without OHG drugs. Conversely, current clinical practice is adherent to Eritrean National Treatment Guideline Edition 2003 [19] and Treatment Algarithm of Internationl Diabetes Federation Eritrea [20].

Discussion

The prevalence of type II DM was slightly higher in females than in males and this result is similar to the report found in WHO Eritrean country profile 2012 [7]; NCDs mortality rate was higher in females (6.3) than males (5.6). But current result was contrary to other observations that showed globally, diabetes prevalence is similar in men and women, but it is slightly higher in men <60 years old and in women at older ages [10]. Hypertension was the commonly seen comorbid disease and this result is supported by many other research from the US and India [11, 12]. Monotherapy was prescribed to many patients. Sulphonyl ureas and Metformin were prescribed to almost all diabetic patients. The present findings are consistent with the research of Patel et al., [13] confirmed that many patients were prescribed sulphonylurea class of drugs (483, 47%) followed by biguanides (246, 24%) and another study from the United Stateshad shown a high utilization of the second-generation sulphonylurea that are Glibenclamide and Glimipride [14]. The present study found neither three drug combination nor other oral hypoglycemic drugs such as Thiazolidinedione, Alpha glycosidase inhibitor, DPP4 inhibitors and incretin mimetics. Besides, Sulphonyl ureas were prescribed to a lot of patients even to patients of poor glycemic control. This result was contrary to the report of United Kingdom Prospective Diabetes Study (UKPDS) which says, insulin secretoguge is effective during initial stage of type II DM but their efficacy lost over a period, necessitating the introduction of combination therapy [16] and it is agreed by another study in which 53% of newly diagnosed type 2 diabetics initially treated with sulfonylureas subsequently shifted to an additional treatment within 6 years to maintain glycemic control [15].

The present study reveals the high FPG reduction of Glibenclamide and Metformin combination and this resulting conflict with other research showed that Metformin-Glimepiride combination resulted in significantly greater reductions in HbA1C and fasting plasma glucose compared with metformin plus Glibenclamide [17]. Many research supported that the combination oral hypoglycaemic drugs resulted in superior glycemic control than monotherapy and short acting insulin [17, 18] and it is proved once again in this study. In view of the fact that the prevalence of Type II DM is high in Eritrean population and it is crucial to control glycemia to circumvent diabetic complications. In conclusion, A combination therapy proved to be effective, modest on glycemic control than a monotherapy. Glibenclamide and Metformin were used usually as single or multiple therapy and show better efficacy. However, currently available oral hypoglycaemic drugs may not give the prescribing flexibility to physicians based on patient's

demographics, comorbid conditions and other patient related factors and this problem will be solved by practicing add-on therapy.

Acknowledgement

The authors sincerely thank Medical Director of Helibet Referral Hospital, Asmara. We also thank Prof. Raouf Hamed/ Associate Research Dean and Prof. Ashok Sharma/ School Head of Pharmacy, Amara college of Health Sciences, Asmara for their valuable guidance and support.

Limitations

The limits of this study include the small sample size which may not represent the treatment pattern of the whole country. However, this could be used as a base for future studies. Since it is retrospective nature, there are chances for change of prescribed drugs.

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Table 1. Patient demographics at baseline

S.No	Parameters	No-of patient *n=200(* %)
1	**Sex**	
	Male	97 (48.5)
	Female	103 (51.5)
2	**Age**	
	Below 60	120 (60)
	Above 60	80 (40)
3	**Mean age**	
	Male	57.16 ± 10. 204
	Female	55.91 ± 7.819
4	**Comorbid**	
	Hypertension	49 (24.5)
5	**Treatment**	
	Monotherapy	135 (67.5)
	Combination therapy	65 (32.5)

Figure 1. Drugs prescribed in regimen for Type II diabetes patients

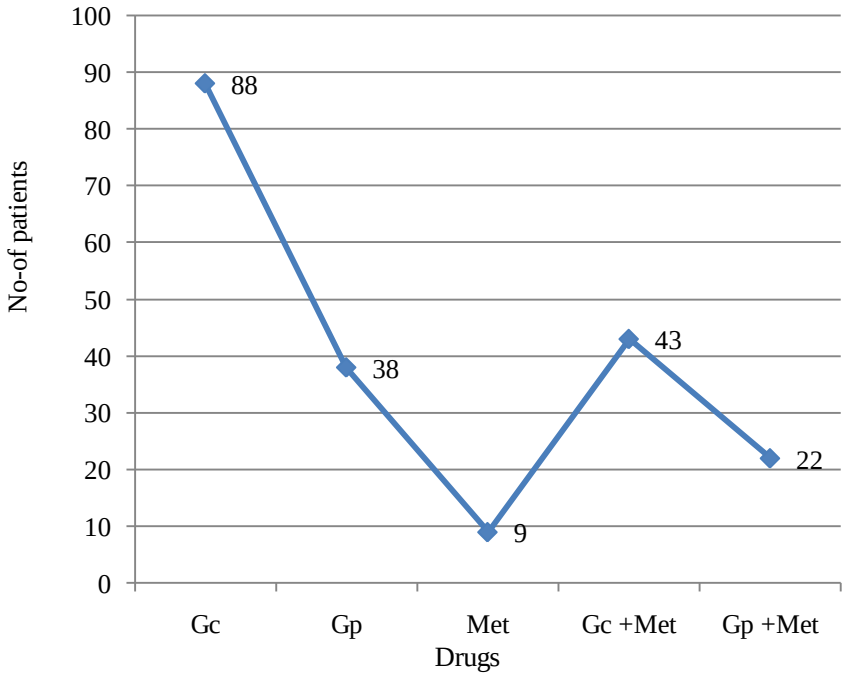

Table 2. FPG reduction of various oral hypoglycemic drugs

FPG	Monotherapy	Combination therapy
Baseline	170.39±56.23	242.16±63.128
IInd FU	126.30±35.60	164.50±43.088
Mean Difference	44.08±20.67	78.66±20.040*
	Glibenclamide	Glibenclamide + Metformin
Baseline	176.829±55.482	222.023±63.971
IInd FU	132.898±36.437	163.351±41.382
Mean Difference	44.131±18.999	58.672±22.589*
	Glimipride	Glimipride+ Metformin
Baseline	161.289±54.822	192.909±56.699
IInd FU	115.656±33.047	177.411±45.476
Mean Difference	45.633±21.775	15.498±11.223
	Metformin	
Baseline	146.111±55.42	
IInd FU	106.2±7.0256	
Mean Difference	39.911±48.398	

FPG –Fasting Plasma Glucose, FU –Follow up, GC – Glibenclamide, GP – Glimipride, Met – Metformin, *Significant