



Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx



Review

Controversy of oral hypoglycemic agents in type 2 diabetes mellitus: Novel move towards combination therapies

Abhijit A. Ghadge, M.Sc., Aniket A. Kuvalekar, Ph.D.*

Diabetes Laboratory, Interactive Research School for Health Affairs (IRSHA), Bharati Vidyapeeth Deemed University, Pune-Satara Road, Pune, Maharashtra, 411043 India

ARTICLE INFO

Article history:
Available online xxx

Keywords:
Diabetes mellitus
Medicinal plants
Omega-3 fatty acids
Oral hypoglycemic agent

ABSTRACT

Aim: As diabetes mellitus is multi-factorial disease, use of several oral hypoglycemic agents (OHAs) is the main stay of pharmacological treatment. The treatment has become more challenging and controversial as OHAs are heterogeneous in their mode of action that causes unwanted side effects. Complementary approaches such as use of medicinal plants and dietary polyunsaturated fatty acids (PUFA) with hypoglycemic and hypolipidemic activities are therefore imperative. A vast literature has independently documented the effects of OHAs, medicinal plants and PUFA for management of diabetes. In the present article, we have reviewed the current literature to describe the effects of commonly used OHAs, their mechanisms of action and reported controversies. The antidiabetic potential of herbs and/or formulations and omega-3 PUFA with its potential benefits and mode of action is also discussed.

Methods: PUBMED, MEDLINE, Cochrane Library etc., were searched for relevant articles using appropriate terms (until February 2015). Human and animal studies were selected for the review. Data extraction was carried out by one author and checked by second author.

Results: There is still controversy over the safety profile of OHAs. Medicinal herbs with hypoglycemic activities are increasingly sought because of its natural origin, active constituents and minimal side effects. The current literature suggests that supplementation with PUFA improves macro- and microvascular complications.

Conclusion: There is a need for best possible individualized treatment based on variations in biochemical parameters with combinational therapy of nutritional/herbal supplementations. Such a combination may be helpful for better management of diabetes and its complications.

© 2016 Diabetes India. Published by Elsevier Ltd. All rights reserved.

Contents

1. Introduction	00
2. Oral hypoglycemic agents (OHAs)	00
2.1. Biguanides	00
2.1.1. Mechanism of action	00
2.1.2. Side effects	00
2.2. Thiazolidinediones	00
2.2.1. Mechanism of action	00
2.2.2. Side effects	00
2.3. Sulfonylureas	00
2.3.1. Mechanism of action	00
2.3.2. Side effects	00
2.4. Alpha-glucosidase inhibitor	00
2.4.1. Mechanism of action	00
2.4.2. Side effects	00

* Corresponding author.
E-mail address: kuaniket@gmail.com (A.A. Kuvalekar).

3.	Other therapeutic agents with anti-hyperglycemic effects	00
3.1.	Angiotensin II type 1 receptor (AT1) blocker	00
3.1.1.	Mechanism of action	00
3.1.2.	Side effects	00
3.2.	Hydroxymethylglutaryl-CoA (HMG-CoA) reductase inhibitor	00
3.2.1.	Mechanism of action	00
3.2.2.	Side effects	00
4.	Alternative/complementary therapies	00
4.1.	Ayurvedic therapies	00
4.1.1.	Single herbs	00
4.1.2.	Herbal formulations	00
5.	Novel move towards combinational therapy with omega 3 fatty acids	00
6.	Conclusions	00
	Declaration of interest	00
	Acknowledgements	00
	References	00

1. Introduction

Diabetes mellitus is defined as a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both [1]. Type 1 diabetes mellitus is an autoimmune disease where immune system attacks and destroys the β cells in the pancreas with little or no insulin production [2]. In type 2 diabetes (T2DM), also known as non-insulin-dependent diabetes mellitus, pancreas usually produces enough insulin but it cannot be effectively utilized by target organs, leading to a condition known as insulin resistance. Around 90–95% of the diabetic subjects are type 2 diabetic [3].

Diabetes is an increasingly important condition globally [4] where Asia, in particular is experiencing a rapidly emerging diabetes epidemic [5]. According to the World Health Organization (WHO) criteria, the prevalence of clinically diagnosed diabetes is reported to be 5.6% and 2.7% among urban and rural India, respectively [6]. A nationwide survey across India showed 1.3% prevalence of self-reported T2DM which is more in men (1.5%) than women (1.0%) [7]. A study in Western India indicated age standardized prevalence of 8.6% in urban [8] and 9.3% in rural Maharashtra [9]. In view of this, we carried out a pilot survey in Western Maharashtra and found that awareness about regular health check-up was quite low (20%–35.71%) and about 12% of subjects, who never had medical check-up, had at least two symptoms of metabolic disorders suggesting an urgent need for raising awareness about diabetes in general population [10].

Currently there are several oral hypoglycemic agents available for the treatment of diabetes mellitus recommended by American Diabetes Association (ADA) and European Diabetes Association for the Study of Diabetes (EASD). These drugs are administered orally and are thus also called oral hypoglycemic agents (OHAs) or oral antihyperglycemic agents. Among these, metformin is considered as first-line treatment [11] and sulfonylureas, thiazolidinediones (TZDs), dipeptidyl peptidase-IV (DPP-4) inhibitors, glucagon-like polypeptide-1 (GLP-1) agonists and insulin are considered as second-line treatment [12]. These treatments are used either alone or in combination with other drugs to achieve better effects. Treatment is based on the interplay of patient's biochemical parameters and available therapeutic options [13]. With a wide range of newly available pharmacological agents, diabetes treatment has become more challenging and controversial owing to their undesirable side effects [11,14]. It therefore is of immense importance to have an excellent understanding of the mechanism of action as well as side effects of these OHAs, in order to provide individualized treatment to diabetic patients. Several systematic reviews have independently documented the potential beneficial

effects of OHAs, medicinal plants and PUFA for the treatment/management of diabetes. Aim of this article is to present a recent overview of the commonly used OHAs, their efficacy with mechanisms of action and reported side effects. In addition to this, we have also discussed the current literature that provides insights on alternative and/or complementary therapies available for the management of T2DM.

2. Oral hypoglycemic agents (OHAs)

With the discovery of new therapeutic options, available treatment modalities with OHAs have got significant choice for the clinicians. Most commonly prescribed OHAs are listed in Table 1.

2.1. Biguanides

Metformin (dimethyl-biguanide) is approved by the U.S. Food and Drug Administration (USFDA) to treat T2DM and its safety profile is probably superior to those seen with other insulin sensitizing drugs [15]. Metformin's first line position was strengthened by the United Kingdom Prospective Diabetes Study (UKPDS) observation, where it has shown to reduce the diabetic complications and mortality by 32% and 42% respectively [16].

Biguanides are known to reduce hepatic glucose production and increase the peripheral glucose uptake in skeletal muscles. Reports suggest favorable effect of metformin on body weight, hyperinsulinaemia, lipid profile, arterial vascular disease, removal of small blood clots and endothelial dysfunction [15]. Metformin is

Table 1
Classification and commonly prescribed OHAs.

Sr. No.	Class	Drug
1	Biguanides	Metformin
2	Thiazolidinediones (TZDs)	Pioglitazone Rosiglitazone Troglitazone
3	Sulfonylureas	First generation: Chlorpropamide Tolazamide Tolbutamide Second generation: Glimepiride Glipizide Glyburide
4	Alpha – glucosidase inhibitor	Voglibose

Download English Version:

<https://daneshyari.com/en/article/8658985>

Download Persian Version:

<https://daneshyari.com/article/8658985>

[Daneshyari.com](https://daneshyari.com)