An Observational Study of the Antidiabetic Activity of Berberine in Newly Diagnosed Type 2 Diabetes Mellitus Patients

Background
Suboptimal glycemic control is a common situation in diabetes, regardless of the wide range of drugs available to achieve glycemic targets. There is in fact a growing body of literature on plants used for the treatment of diabetes. In this respect, in the past few years, attempts were made to use natural plant products for the treatment of patients with diabetes. Berberine is a commonly available as a nutraceutical and it is a potential candidate for diabetes.

Methods and Results
A total of 30 newly diagnosed type 2 diabetes mellitus patients were included in the study after obtaining their informed written consent. They were divided into two groups (n = 15 each), receiving either metformin 500 mg/12 h or berberine 500 mg/12 h p.o. for 12 weeks. No other antidiabetic drugs were given. Therapeutic life style measures were common in both groups. Physical examination and estimation of laboratory parameters were done at baseline and after 12 weeks. Laboratory parameters estimated were fasting blood glucose level (FBG), post prandial blood glucose level (PPBG), glycated hemoglobin (Ghb), lipid profile, serum alanine transferase and serum creatinine. Berberine treatment significantly reduced FBG, PPBG, Ghb levels and there was significant improvement in lipid profile. The results were comparable to those with metformin.

Conclusion
Berberine (500 mg twice daily) may be a useful antidiabetic drug.

Keywords
antidiabetic activity, berberine, type 2 diabetes mellitus

INTRODUCTION
Type 2 diabetes mellitus (T2 DM) is a worldwide health threat and treatment of this disease is unsatisfactory, inspite of the availability of effective medications. All of the existing oral hypoglycemic agents have subsequent failure after long term control of blood glucose. Berberine is a natural alkaloid (Fig. 1) (molecular formula of C_{19}H_{19}N_{4}O_{3} and molecular weight of 353.36) and the main active component of an ancient Chinese herb *Coptis chinensis* Franch, which has been used to treat diabetes for thousands of years. Berberine is an over-the-counter (OTC) drug, which is used to treat gastrointestinal infections in China. Berberine hydrochloride (B-HCl·nH_{2}O)—the most popular form of berberine, is used in this study. The chemical structure of berberine and related isoququinoline alkaloids is quite different from the other commonly used hypoglycemic agents such as sulphonyl ureas, biguanides, thiazolidinediones and acarbose. Hence, if the efficacy and safety of berberine are confirmed, it can serve as a new class of antidiabetic medication. Several clinical investigations of berberine in the treatment of diabetes reported that fasting blood glucose (FBG) concentration in 60 patients with type 2 diabetes was reduced from 11.6 to 6.6 mmol/l for 1–3 months, when treated with berberine (0.3–0.5 g daily three times)\(^2\).

Xie et al. (2005) found that, when berberine (0.3–0.5 g, three times daily), was administered to 40 patients of type 2 diabetes for 2 months without changing their previous therapy, FBG and prandial blood glucose (PPBG) were reduced by 21 and 27% respectively\(^3\). Wei et al. (2004) reported that the treatment with berberine (0.5 g daily three times daily) for 2 months in 30 patients of type 2 diabetes with fatty liver decreased fasting glucose, triglyceride and total cholesterol concentration by 31, 40
and 23% respectively, and was associated with decrease in serum alanine aminotransferases and aspartate aminotransaminase concentrations⁴.

However, there are few studies comparing it with metformin, the golden standard, in real life situation. Hence, this study has been conducted. The present study bridges the previous mechanism research with the clinical observations (Tables 1, 2).

**AIM AND OBJECTIVES**

Aim: To evaluate the antidiabetic activity of berberine with following objectives:

1. To assess the antidiabetic activity of berberine.
2. To compare the antidiabetic effect of berberine with metformin.

**PATIENTS AND METHODS**

**Study design**

This was an open labelled, observational and single centre study, approved by local Institutional Ethics Committee. Patients attending the OPD of Dhanashree Hospital, New Sangvi, Pune; were screened for type 2 DM. Newly diagnosed patients of either sex and age: 25–70 years were included in the study after obtaining their informed written consent. Initial screening included a medical history, physical examination and laboratory tests viz. HMG, BSL-F and post prandial (PP), SALT, serum creatinine, serum lipid profile, glycated hemoglobin (GHb) and urine routine analysis. Then they received either metformin (500 mg bid) or berberine (500 mg bid) after food for 12 weeks. BSL was repeated at monthly intervals while all initial tests were repeated at the end of 12 weeks. Adverse effects, if any, were assessed with the help of a questionnaire. Compliance was assessed by return tablet count.

**Exclusion criteria**

Patients with the following were excluded: (1) Liver and renal dysfunction, (2) cardiac disease, (3) psychiatric disease, (4) severe infection and (5) pregnancy. No other drugs like statins or antiHT drugs were allowed.

**Statistical analysis**

The data was analysed by Student’s ‘t’-test; unpaired ‘t’-test was used to compare in between the groups. The P value of <0.05 was considered as statistically significant.

**RESULTS**

Forty patients were screened; out of which 30 patients completed the study (Fig. 2). There were 10 dropouts, 6 had severe gastrointestinal discomfort (4-metformin, 2-berberine) and 4 (1-metformin, 3-berberine) were lost without any visits. The data of 30 participants were analysed (Figs. 3, 4).

**DISCUSSION**

The results of our study indicate that berberine, in the dose of 500 mg twice daily after food for 12 weeks...
were well tolerated; the side effects were mainly gastrointestinal and minor. This is consistent with earlier reports.

A recent meta-analysis of 14 randomised trials involving 1,068 patients of T2 DM, revealed that treatment with berberine resulted in significant hypoglycemic and antidyslipidemic benefits. The effects did not differ from those obtained by the standard hypoglycemic drugs such as metformin, glipizide or rosiglitazone.

The exact mechanism of action of berberine is not known. It has been reported to affect glucose metabolism via multiple mechanisms like increase in insulin receptor expression, stimulation of insulin secretion by enhancing GLP-1 activity in a glucose dependent manner from the pancreas, activation of AMPK (5′-AMP-activated protein kinase)—intracellularly, enhancement of glucose uptake by upmodulation of glucose transporter type 4 (GLUT4), decrease in intestinal glucose absorption by inhibition of α-glucosidase and upregulation of low density lipoprotein receptor expression.

The limitations of our study are: it is an open, observational study, with small number of patients, single dose regimen and of short duration. The efficacy of berberine needs to be tested in much larger population with long term double blind randomised multicentric studies.

To summarise, berberine is an effective and safe oral hypoglycemic agent. It may serve as a new drug candidate in treatment of type 2 diabetes.

CONCLUSION

Berberine in the dose of 500 mg twice daily was found to be useful to improve the glycemic parameters in this small observational study. The effect was comparable to metformin. And hence, berberine may be useful as an additional antidiabetic drug.

REFERENCES

1. Ni YX. Therapeutic effect of berberine on 60 patients with type II diabetes mellitus and experimental research. Zhong Xi Yi Jie He Za Zhi. 1988;8:711–713.


