Effect of Bromocriptine Mesylate as Add-On Therapy in Obese Type 2 Diabetes Mellitus Patients

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Abstract

Six months administration of bromocriptine mesylate significantly decreased glycated hemoglobin (HbA1c), fasting blood sugar, postprandial blood sugar, and weight of 22 Indian obese patients with type 2 diabetes mellitus with no serious adverse events. Therefore, the novel mechanism of action, efficacy and acceptable safety profile makes this drug an attractive option for treatment of obese type 2 diabetic patients.

Keywords: T2DM, Bromocriptine mesylate, HbA1c

Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder, caused by insulin resistance, impaired β-cell function, and multiple other metabolic abnormalities. Obesity is a well-established risk factor for type 2 diabetes (1), with 60-80% of T2DM patients are obese. Bromocriptine mesylate, an ergot derivative, is a sympatholytic D2-dopamine agonist. It exerts inhibitory effects on serotonin turnover in the central nervous system (CNS) and reduces plasma glucose, triglycerides, and Free Fatty Acid (FFA) levels. The utility of bromocriptine in diabetic patients has been recognized, based on its activity in modulating central glucose and energy metabolism pathways (2,3). Bromocriptine is believed to augment low hypothalamic dopamine levels and inhibit excessive sympathetic tone within the CNS, resulting in a reduction in postmeal plasma glucose levels, due to enhanced suppression of hepatic glucose production (4).

The role of bromocriptine mesylate has been studied in more than 4300 patients with T2DM. Recently, the drug has been approved by the US FDA for the treatment of T2DM (5). However, limited data is available in Indian population. So, the present study is undertaken to assess the efficacy and safety of bromocriptine mesylate as an add-on therapy in T2DM patients.

Materials and Methods

Total 60 obese T2DM patients were evaluated to enroll 22 eligible patients from the outpatient clinic at a centre in central India in a 6-months period (May 2011 to December 2011). Eligibility criteria were a fasting plasma glucose (FBS) concentration between 140 and 240 mg/dl; glycated hemoglobin concentrations (HbA1c)>7%; stable body weight for at least 3 months before the enrollment in the study, a BMI between 25-35 kg/m^2 for both men and women, and no evidence of cardiac, hepatic, renal, or other chronic renal diseases as determined by medical history, physical examination and screening laboratory tests. Written informed consents were taken from all the patients. Patients who were on insulin or other anti-diabetic drugs affecting insulin sensitivity were included in the study in order to assess the add-on effect of bromocriptine mesylate. The protocol was approved by the Institutional ethics Committee.

The study was an open-label with the treatment period of 6 months. Primary outcome measure was HbA1c at the end of the treatment (EOT). HbA1c was recorded at the baseline (before the initiation of the treatment and EOT). FBS, post-prandial blood sugar (PPBS) and weight were recorded at the baseline and then at monthly interval till EOT.

Table 1. Baseline characteristics of the study participants

No of patients screened/randomized	60/22
Male/Female [n (%)]	8 (36.36)/14 (63.64)
Weight (kg)	76.50 ± 10.61
BMI (Kg/m^2)	28.75 ± 2.87
HbA1c (%)	7.55 ± 0.53
FBS (mg/dl)	164.50 ± 33.99
PPBS (mg/dl)	230.32 ± 55.13

Bromocriptine mesylate was started as 0.8 mg once a day and then the dose was increased to 0.16 mg on second follow up visit. Safety was assessed in terms of systemic adverse effects by questioning patients at each visit and by clinical and biochemical examination at the end of the study.

Statistical analysis

For continuous variables, data are presented as mean ± SD. Paired Student's t test was applied for Pre Vs Post comparison. Significance level was set at $p< 0.05$.

Results

Baseline characteristics of the patients are summarised in Table 1**.**

Efficacy

HbA1c: Mean HbA1c at the baseline was 7.55 mg/dl, which was lowered to 6.89 mg/dl and the reduction was statistically significant (P<0.001). The 6-months change from baseline was 0.66 mg/dl. Nine patients (41%) showed HbA1c reduction ≥1%.

FBS: Mean FBS at the baseline was 164.50 mg/dl which was lowered to 130.05 mg/dl. The reduction was statistically significant (*P*<0.01). The 6-months change from baseline was 34.45 mg/dl. Fourteen (64%) and 3 (14%) patients showed FBS reduction ≥30 mg/dl and ≥ 50 mg/dl, respectively.

Table 2. Mean values of the parameters at baseline and at the end of treatment in the study participants.

Parameters	At baseline (Mean ± SD)	At EOT (Mean ± SD)	Mean difference	*P*-value
Weight (kg)	76.50 ± 10.61	75.76± 10.82	0.74	0.001
HbA1c (%)	7.55 ± 0.53	6.89 ± 0.72	0.66	0.001
FBS (mg/dl)	164.50 ± 33.99	130.05 ± 29.59	34.45	0.001
PPBS (mg/dl)	230.32 ± 55.13	200.36 ± 46.43	29.95	0.001

*** *Paired t test* is applied. *P*-value <0.05 considered significant.**

PPBS: Mean PPBS at the baseline was 230.32 mg/dl which was decreased to 200.36 mg/dl. The reduction was statistically significant. The 6-months change from baseline was 29.95 mg/dl. Six (27%) and 3 (14%) patients showed PPBS reduction ≥ 30mg/dl and ≥ 50mg/dl, respectively.

Weight: Statistically significant weight reduction was seen from 76.50 kg at baseline to 75.76 kg at the EOT (Table 2).

Safety

Reported adverse events of bromocriptine mesylate were tastelessness (14%), dizziness (20%) and increased frequency of urination in morning (24%). All the adverse events were mild and seen in morning hours only.

Conclusion

The novel mechanism of action, good efficacy and acceptable safety profile make it an attractive option for the treatment of Indian patients with obese T2DM.

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