Original Research Article

Comparative study of hypoglycemic effects of oral vildagliptin and voglibose on fasting blood sugar level in albino rats

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ABSTRACT

Background: Diabetes mellitus is a metabolic disorder in which there is increased blood sugar level, glycosuria, dyslipidemia and sometimes ketonemia occurs. Increased blood sugar level leads to characteristic symptoms such as polydipsia, polyurea, blurring of vision, polyphagia and weight loss.
Methods: Healthy male Wister rats weighing between 150-250 gm were taken. Total 2 groups A and B were prepared and each group contains 6 animals. Group A was administered voglibose as 0.6 mg/70 kg body weight. Group B was administered vildagliptin as 100 mg/70 kg body weight. Diabetes was induced in group A and B by administration of 120 mg/kg body weight of nicotinamide and 60 mg/kg body weight of streptozocin intraperitoneally. Streptozocin was administered after 15-20 minutes of administration of nicotinamide. After 72 hours of streptozotocin injection, fasting blood glucose level was determined and induction of diabetes was confirmed. The fasting blood samples were collected from all the groups on further days 7, 14, 21 and 28 day to determine the glucose level by glucometer.
Results: The decline in fasting blood sugar level by voglibose was 36.4% on day 7, 40.2% on day 14, 43.94% on day 21 and 46.4% on day 28. The reduction in Fasting blood sugar level by vildagliptin was 49% on day 7, 52.25% on day 14 and 54% on day 21 and 28. Thus in group B rats, decline was maximal on day 7 and little fall was recorded on subsequent days. It suggests good efficacy as vildagliptin normalized the blood glucose level effectively.
Conclusions: Vildagliptin was found significantly more effective in lowering fasting blood glucose level than voglibose.

Keywords: Glycosuria, Dyslipidemia, Ketonemia, Charcot joint, Polydipsia, Polyurea, Polyphasia

INTRODUCTION

Diabetes mellitus refers to a group of common metabolic disorders that share the phenotype of hyperglycemia.[1] Severe distinct type of diabetes mellitus are caused by a complex interaction between genetics and environmental factors which involve insufficient insulin secretion, increased glucose production, reduced responsiveness to endogenous or exogenous insulin leading to insulin resistance and abnormalities in protein and fat metabolism.[2] The resulting hyperglycemia may lead to characteristic symptoms and metabolic abnormalities such as polydipsia, polyurea, blurring of vision, polyphagia and weight loss. Long term complication of diabetes include retinopathy with potential loss of vision; nephropathy leading to renal failure; peripheral neuropathy with risk of foot ulcer, amputation and Charcot joint and autonomic neuropathy causing gastrointestinal, genitourinary and cardiovascular symptoms and sexual dysfunction.[3] The prevalence of diabetes for all age groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030.[4] As per the international

diabetes federation (2013), approximately 50% of all people with diabetes live in just three countries: China (98.4 million), India (65.1 million) and the USA (24.4 million).[5] According to "the international diabetes federation", the worldwide prevalence of diabetes has risen over the past two decades, from an estimated 30 million cases in 1985 to 285 in 2010 to 438 million by 2030.[6] The international diabetes federation (IDF) reports a projected prevalence of 70 million patients in India by the year 2025, and the world health organization (WHO) estimates that India will have 80 million cases of diabetes by 2030.[7] The prevalence of diabetes is higher in men than women, but there are more women with diabetes than men.[8] Voglibose is a complex oligosaccharide which reversibly inhibits α-glucosidase, the final enzyme for the carbohydrate digestion present in the brush border of the small intestine where it slows down and decreases digestion and absorption of sucrose and polysaccharides like starch. Voglibose reduces HBA1c by 0.5-0.8%, fasting glucose by ~1 mM and postprandial glucose by 2.0-2.5 mM.[9] vildagliptin, a dipeptidyl peptidase-1(DPP-4) inhibitor, decreases the inactivation of glucagon like peptide-1(GLP-1) thereby increasing its secretion, accompanied with a decrease in that of glucagon. Important vildagliptin-induced beneficial effects in type 2 diabetes mellitus (T2 DM) include significant reduction in HB1Ac (0.8-1.0%) and both fasting and postprandial plasma glucose along with marked improvement in lipid profile as well.[10]

The current study was conducted with aims and objectives were to compare the hypoglycemic effect of voglibose and vildagliptin.

METHODS

Place of study

The entire experiment was carried out in postgraduate laboratory department of pharmacology and therapeutics Rajendra institute of medical sciences, Ranchi.

Study design

Randomized, open label, interventional, comparative, diabetic animal model study was used as study design.

Study duration

The study carried out for total six months from 1st October 2014 to 31st march 2015.

Animals used

Healthy male Wister rats weighing between 150-250 gm were taken for our present study. The animals were kept in clean and dry cages, with 12:12 hours light-dark cycle at room temperature (~24-28[0]C) and humidity. They were acclimatized to the available housing condition for a period of 1 month. Animal room was maintained with adequate light and ventilation. Rats were fed with standard laboratory diet consisting of soaked black gram (Kala Chana) and soyabean. The whole experiment was conducted in accordance with ethical norms approved by institutional animal ethics committee (IAEC) guidelines.

Inclusion criteria

The inclusion criteria included the healthy and active in their cage animals. Animals were male Wister rats. Weight of the animal used was 150-250 gm. Fasting blood sugar before the initiation of study was within the range of 200-250 mg/dl.

Exclusion criteria

Diseased and inactive rats were excluded from the study. Rats with weight less than 150 grams and above 250 gm were excluded from the study. Rats with fasting blood sugar under 200 mg/dl and above 250 mg/dl were considered as improperly diabetic and excluded from the study.

**Table 1: Groups of animals (A and B- six rats in each).**

Group	Rats	Drugs	Dose/day
A-Voglibose	6	Voglibose	0.6 mg/70 kg body weight
B-Vildagliptin	6	Vildagliptin	100 mg/70 kg body weight [(100 mg*0.018)/ml]

Administration of drugs with doses

Total 2 groups A and B were prepared and each group contains 6 animals. Group A was administered voglibose as 0.6 mg/70 kg body weight. Group B was administered vildagliptin as 100 mg/70 kg body weight. Diabetes was induced in group A and B by administration of 120 mg/kg body weight of nicotinamide and 60 mg/kg body weight of streptozocin intraperitoneally. Streptozocin was administered after 15-20 minutes of administration of nicotinamide. After 72 hours of streptozotocin injection, fasting blood glucose level was determined and induction of diabetes was confirmed. The fasting blood samples were collected from all groups on further days 7, 14, 21 and 28 day to determine the glucose level by glucometer.

Statistical analysis

Statistical analysis of data was carried out by employing analysis of variance (Snedecor and Cochran, 1967). One way ANOVA test was used to compare the effect of drugs on different group the effect. Tukey's HSD test was used for post-hoc analysis of significant overall differences.
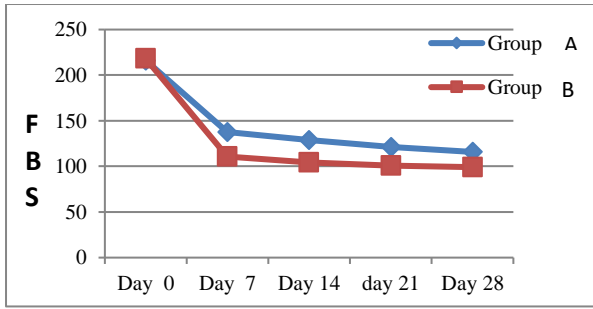
Figure 1: Graphical representation of day by day FBS values in group A and B.

RESULTS

Table 2 gives the value of FBS in group A rats that were induced diabetes and administered voglibose dissolved in 1% gum acacia suspension for the entire duration of experiment., and later on day 7, 14, 21 and 28 the FBS decrease. The decline in FBS was 36.4% on day 7, 40.2% on day 14, 43.94% on day 21 and 46.4% on day 28.

Table 3 gives the value of FBS in group B rats that were induced diabetes and administered vildagliptin in 1% gum acacia for the entire duration of experiment. This table shows FBS reading of moderate hyperglycemia (209-228) on day 0, further on day 7, 14, 21 and 28, the FBS gradually decreases. Here the reduction in FBS was 49% on day 7, 52.25% on day 14 and ~54% on day 21 and 28. Thus in group D rats, decline was maximal on day 7 and little fall was recorded on subsequent days. It suggests good efficacy as vildagliptin normalized the blood glucose level effectively.

Table 4 compares the FBS voglibose with vildagliptin treated group. Test group A and B have mean difference of 2.0 which showed insignificant relationship on day 0. Reduction in FBS was more in group B (~54%) than group A (~46.4%) on day 28. Group B proved its better efficacy and maintenance of normoglycemia in comparison to group A. Also, it is clearly depicted by significance value of 0.000^* on day 7 to day 28 that group B is superior to group A.

Table 2: Value of FBS on 0, 7th, 14th, 21st and 28th day in group A. (Diabetic rats that were treated with voglibose).

Diabetic rats	Day 0	Day 7	Day 14	Day 21	Day 28
Rat 13	214	138	122	120	118
Rat 14	211	133	124	113	107
Rat 15	228	146	133	121	123
Rat 16	209	129	131	126	119
Rat 17	223	139	135	128	116
Rat 18	212	140	130	119	112
Mean	216.1	137.5	129.17	121.17	115.83
SD	7.574	5.891	5.115	5.345	5.636

Table 3: Value of FBS on 0, 7th, 14th, 21st and 28th day in group B. (Diabetic rats that were treated with vildagliptin).

Diabetic rats	Day 0	Day 7	Day 14	Day 21	Day 28
Rat 19	211	109	100	97	97
Rat 20	220	113	109	107	103
Rat 21	217	109	102	99	97
Rat 22	229	117	107	102	100
Rat 23	223	110	104	98	96
Rat 24	209	107	103	99	102
Mean	218.1	110.83	104.17	100.83	99.17
SD	7.494	3.601	3.312	3.670	2.927

Table 4: FBS in group A and group B.

Days	Group A	Group B	Mean difference	Sig.
Day 0	216.1±7.574	218.1±7.494	2.000	0.982**
Day 7	137.5±5.891	110.83±3.601	26.667	0.000*
Day 14	129.17±5.115	104.17±3.312	25.000	0.000*
Day 21	121.17±5.345	100.83±3.670	20.833	0.000*
Day 28	115.83±5.636	99.17±2.927	16.667	0.000*

DISCUSSION

Statistical interpretation of this study shows that vildagliptin have greater glucose lowering effect than voglibose. Also, mean FBS value of voglibose, vildagliptin was 115.83 mg/dl, 99.17 mg/dl on day 28. Vildagliptin is potent DPP-4 inhibitor which deactivates the main GLP-1 consuming enzyme, dipeptidyl peptidase-4 and enhance GLP-1 level during each meal, similarly voglibose also increases the release of the glucoregulatory hormone glucagon like peptide-1 (GLP-1) into the circulation which contribute to their glucose lowering effect, may have boosting effect on the gliptins.[11] They not only reduce fasting and postprandial glucose level by increasing insulin secretions but also simultaneously sensitize alpha cells to inhibit glucagon secretion.[12] α glucosidase inhibitors have common side effects of malabsorption, soft stools, flatulence, abdominal pain or discomfort but these side effects are minor with voglibose and not clinically significant.[13] Vildagliptin, as an inhibitor of DPP-4 enzyme may have potential harmful effects on the immune system, resulting in a possible risk for infections and may cause angioedema by affecting substance P and neurokinin level.[14]

CONCLUSION

Both voglibose and vildagliptin lowered fasting blood glucose towards normal range when used individually. Vildagliptin was found significantly more effective in lowering fasting blood glucose level than voglibose.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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