

Original Article

EFFECT OF FAMOTIDINE ON HYPOGLYCAEMIC ACTIVITY OF GLIBENCLAMIDE

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ABSTRACT

Objective: To study the effect of famotidine (H₂ receptor antagonist) in combination with Glibenclamide on the blood sugar level in rabbits.

Methods: Six albino rabbits were taken for the study. Glibenclamide was administered to each rabbit as a single drug therapy on day 1, while was co-administrated with Famotidine to each rabbit as a combinational drug therapy on day 7. Famotidine was administered to each rabbit from day 2 to day 6 as a single drug therapy. Blood sugar levels were estimated on day 1 and on day 7 at 0, 1, 2, 4, and 6 h.

Results: The mean blood sugar level readings at 0, 1, 2, 4 and 6 h on day 1 were 91.1, 79.7, 70.6, 61.8 and 66.5 mg% and on day 7 were 91.1, 78.5, 69.6, 60.6 and 64.9 mg%, respectively. When blood sugar level on day 1 and 7 were compared, there was. no significant change in any of the readings after co-administration of Glibenclamide and Famotidine.

Conclusion: Famotidine did not produce any significant reduction in Blood sugar level when it was co-administered with glibenclamide

Keywords: Famotidine, Glibenclamide, Hypoglycaemic, Blood sugar

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INTRODUCTION

Type 2 diabetes mellitus is a chronic metabolic disorder with increasing prevalence, characterized by impaired insulin secretion and resistance. Sulphonylureas such as Glibenclamide are commonly prescribed but carry the risk of hypoglycaemia [1]. Patients often require polypharmacy, including H₂ receptor antagonists for gastrointestinal disorders.

Cimetidine is well known to interact with a number of drugs concurrently administered by inhibiting hepatic microsomal enzymes [2]. Adverse effects due to the interaction of Cimetidine with Theophylline, Phenytoin, Warfarin [3-5] have been reported. Co-administration of Cimetidine has been found to influence the hypoglycaemic activity of glibenclamide as reported in study conducted in rabbits [6]. Famotidine is metabolized by the hepatic cytochrome P450 system, but has minimal inhibitory effects on the metabolism of other drugs, making it less likely to cause drug-drug interactions than cimetidine [7].

Limited data exist regarding its interaction with Glibenclamide. Therefore, this study was conducted to evaluate the effect of Famotidine on Glibenclamide-induced hypoglycaemia in rabbits.

MATERIALS AND METHODS

The study was carried out in the experimental room of the central animal house of Government Medical College, Chhatrapati Sambhajnagar. Six healthy albino rabbits of either sex, weighing between 1.6 and 2.1 kg were used in the study. This experimental study was conducted in accordance with the ethical standards for animal research applicable at the time (1999) and was approved by

the Institutional Animal Ethics Committee, Government Medical College, Chhatrapati Sambhajnagar. The CPCSEA guidelines were implemented in subsequent years.

Rabbits were kept for fasting overnight for 18 h. Water was given *ad libitum* and rabbits were kept at temp between 30-33 °C. For oral feeding rabbits, a special rabbit holding box and mouth gag with feeding tube was used. During 7 d of study period, each rabbit was given Glibenclamide and Famotidine as single drug therapy and also as combination therapy as shown below.

Day 1: Glibenclamide

Day 2-6: Famotidine

Day 7: Glibenclamide+Famotidine

Doses of all the drugs were calculated from Fundamentals of Experimental Pharmacology by Ghosh [8]. About 1 ml of blood was collected from marginal ear vein of the rabbits for blood glucose estimation on day 1 and on day 7 at 0, 1, 2, 4, and 6 h. Blood sugar levels were estimated by modified Somogy's method and expressed as milligram per 100 ml (mg %).

Statistical analysis

Mean blood sugar levels were expressed as milligram per 100 ml±standard Deviation (mg %±SD). The Student's t-test was used to test the significance of the difference between treated groups for the blood sugar level on day 1 and day 7 at 0, 1, 2, 4 and 6 h in each treated group and taken as significant at p<0.05.

Table 1: Effect of famotidine on hypoglycaemic activity of glibenclamide in rabbits

Drug	Mean blood sugar level (mg %±SD)				
	0 h	1 h	2 h	4 h	6 h
Glibenclamide (Day 1) (n=6)	91.1±2.03	79.7±1.97	70.6±2.76	61.8±1.90	66.5±2.41
Glibenclamide+Famotidine (Day 7) (n=6)	91.1±0.97	78.5±0.95	69.6±3.14	60.6±2.01	64.9±1.35
P-value	>0.05	>0.05	>0.05	>0.05	>0.05

Value were expressed in mean±SD, Significant at P<0.05

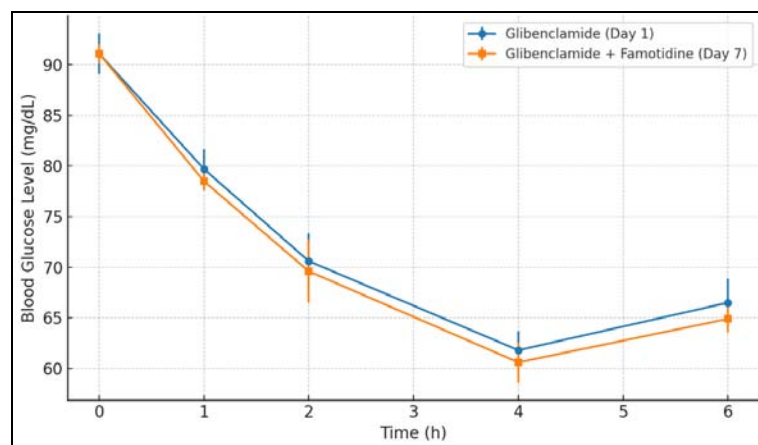


Fig. 1: Mean blood glucose levels (mg%) after glibenclamide alone and with famotidine

RESULTS

The mean blood sugar level readings at 0, 1, 2, 4 and 6 h on day 1 were 91.1, 79.7, 70.6, 61.8 and 66.5 mg% after administration of glibenclamide and on day 7 were 91.1, 78.5, 69.6, 60.6 and 64.9 mg% after administration of Glibenclamide+Famotidine respectively. When mean blood sugar level reading on day 1 and day 7 were compared, there was no significant reduction at 0,1, 2, 4 and 6 h after co-administration of Glibenclamide and Famotidine.

DISCUSSION

This study shows Famotidine did not alter the hypoglycaemic effect of Glibenclamide. In contrast, Cimetidine and Ranitidine potentiates sulphonylurea hypoglycaemia due to P450 inhibition [9, 10]. Famotidine is metabolized by the hepatic cytochrome P450 system, but has minimal inhibitory effects on the metabolism of other drugs, making it less likely to cause drug-drug interactions than cimetidine [7].

No significant effects were found on the biologic disposition of theophylline, warfarin, and other compounds metabolized by the liver cytochrome P450 enzyme system when they are given concomitantly with famotidine [11]. In contrast to cimetidine and ranitidine, famotidine, which possesses a thiazole ring structure, demonstrates minimal or no influence on the hypoglycaemic response to sulphonylureas such as glibenclamide. This lack of interaction may be because, unlike cimetidine and ranitidine, famotidine has a very low affinity for and does not significantly inhibit the hepatic cytochrome P450 (CYP450) enzyme system, which is responsible for the metabolism of many drugs, including sulphonylureas.

Further study published in Journal of clinical pharmacology confirms that therapeutic doses of famotidine do not impair diazepam and desmethyldiazepam kinetics, suggesting that there is no significant kinetic interaction when diazepam and famotidine are administered concurrently [12]. Our results align with this pharmacological profile.

Recent advances in pharmacogenetics highlight the importance of genetic variability in drug metabolism when multiple medications are prescribed. Genetic polymorphisms in cytochrome P450 enzymes, particularly CYP2C9, is known to influence the metabolism of sulphonylureas and other concomitant drugs [13]. Incorporating pharmacogenetic screening before initiating polypharmacy in chronic conditions could help clinicians to predict potential drug-drug interactions, optimize therapeutic efficacy, and minimize adverse effects. Organizations such as Indus Health Plus are actively advancing this field by offering pharmacogenetic testing services, enabling a more personalized approach to medication management and reducing the risk of adverse drug interactions in clinical practice.

CONCLUSION

The co-administration of famotidine with glibenclamide did not result in a statistically significant reduction in blood glucose levels

compared to glibenclamide alone. This finding suggests that famotidine does not potentiate the hypoglycaemic effect of glibenclamide, indicating an absence of clinically relevant pharmacokinetic or pharmacodynamic interaction between the two agents.

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AUTHORS CONTRIBUTIONS

All authors have contributed equally

CONFLICTS OF INTERESTS

The authors declare that they have no conflicts of interest.

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