PRELIMINARY REPORT OF COMPARISON OF GLYBENCLAMIDE AND CHLORPROPAMIDE IN THE TREATMENT OF MATURITY ONSET DIABETES MELLITUS

by
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Introduction:

Glybenclamide (HB 419) is a new hypoglycemic sulphonamide. Pharmacological studies were first published in 1966 (Aumuller et al), and there were further notes issued from laboratories in France and West Germany in 1967-1968.

Pharmacology:

Glybenclamide is a sulphonylurea with a long sidechain. It is a white crystalline powder. The drug is quite remarkably potent on weight basis being approximately 700 times as potent as tolbutamide and at least 50 times as potent as chlorpropamide. It has the same mode of action as tolbutamide, with quantitative but not qualitative differences (Bander 1969). Degranulation of the beta cells has been demonstrated. In Chronic experiments on dogs, the prolonged and persistent stimulation of beta cells has been shown to cause 30% increase in islet cell weight, due to the production of new beta cells (Loubatieres, 1969). The drug has no effect on alpha cells, and it has no effect in the pancreatectomized dog or the alloxan diabetic rabbit (Bander, 1969).

The mechanism of secretion of insulin by HB 419 (Sirek et al, 1969) involves the stimulation of beta adrenergic receptors, activation of the adonyl cyclase system, and a rise in cyclic AMP (cyclic 3'S' adenesine monophospate). The investigations of Soling (1968) support the hypothesis that the therapeutic hypoglycaemic effect of HB 419 depends not only on the betacytotropic effect, but also may be due to a direct effect on liver metabolism.

Purpose of Trial:

To study the efficacy and tolerance of Glybenclamide therapy as also a comparison with chlorpropamide in the short-term treatment of diabetes mellitus of maturity onset.

TYPE OF STUDY

Study Design:

1. Randomized and Crossover trial to get within-subject comparison. Cases were selected from patients attending the diabetic clinic at Rani Pokhari.

2. Type of person selected: 23 adult males and females suffering from maturity onset diabetes. All of them were above 30yrs of age.
3. Exclusion of patients: The following patients were excluded from the study.
 - a) Pregnant Diabetics.
 - b) Those requiring more than 30 units of insulin for control.
 - c) Patients suffering from any acute infections.
 - d) Patients with acetone in the urine.
 - e) Patients with fasting blood sugar of more than 300mg% (Folin Wu).
4. Dose and Method of Administrations:

Every patient was allotted a serial number. Patients receiving any form of hypoglycaemic therapy went through a drug free period of one week before being included in the study. There points glucose tolerance test (Fasting, 1 hour & 2 hours after 100gms glucose load) was performed before the commencement of the trial. Patients put were on either chlorpropamide or glybenclamide. Initially, complete daily dose was administered ten minutes before the morning full meal. 3 point GTT was repeated every week. Depending upon blood sugar values, dose was adjusted by weekly increments of the drug. The aim being to reduce the fasting blood sugar values to 130mg% and that 2hrs after glucose to 150mg% or less. However, no patient received more than 10mg. glybenclamide or more than 750 mgm of chlorpropamide, the excess was administered with the evening meal.

As soon as the aim was achieved the patient was switched over to the other drug. The patients who failed to show even fair control after being with 15mg of glybenclamide or 750mg of chlorpropamide per day for four weeks, were recorded as primary failures and were switched over to the second drug. Initial dose of the second drug was equal in potency to the dose of the first drug being administered to the patient just prior to the switchover. For this purpose 5mg of glybenclamide and 250mg of chlorpropamide were treated as equipotent.

5. Concurrent Treatment:

Patients included in the study did not receive any other antidiabetic drug.

Evaluation of Efficacy:

Efficacy was assessed by three point glucose tolerance test: Fasting blood sugar, and one and two hours blood sugars after 100gm of glucose load, initially and every week thereafter.

Statistical Analysis:

The data were analysed irrespective of the order of administration in the following manner.

a) Degree of Control was judged by the following criteria:

Relation to glucose load	Degree of Control			
	Blood Sugar mg% as determined by Folin Wu method			
	Excellent	Good	Fair	Failure
Fasting	130 or less	171-150	151-170	
1 hour after	130 or less	171-210	211-230	All others
2 hour	150 or less	151-170	171-210	

RESULTS

Total no. of cases—24

Male — — — — — 13

Female — — — — — 11

Age groups (in years)

30 - 39 — — — 2

40 - 49 — — — 8

50 - 59 — — — 8

Male

Maximum age — — — 61 yrs

Minimum age — — — 30 yrs

Weight (in lbs)

maximum — — 168

minimum — — 70

average wt- 120½

Female

Maximum age — 67 yrs

Minimum age — 31 yrs

Fasting Blood Sugar Before Starting Trial

Maximum — — 300 mgm %

Minimum — — 115 mgm %

Duration of Diabetes at start of trial

Maximum — — 11 yrs.

Minimum — — 3 yrs.

Average — — 4.07 yrs

RESULTS

	Excellent	Excellent—to—Good	Good	Fair	Failure
GLYBENCLAMIDE	6	2	3	3	10
CHLORPROPAMIDE	6	3	4	1	9

Over all Response To Glydenclamide — 58.33%

Excellent Good Response — 45.83%

Failure — — — — — 41.66%

Some cases over all Response to Chlorpropamide = 60.87%

Excellent Good Responses — — 56.52%

Failure — — — — — 39.13%

Dose relation of Glybenclamide and Chlorpropamide

For this cases 6, 0, 11 & 22 showing same degree of control with both drugs have been selected.

Case	GLYBENCLAMIDE	CHLORPROPAMIDE
6	15 mgm	750 mgm
9	5 mgm	500 mgm
11	7.5 mgm	250 mgm
22	2.5 mgm	125 mgm

In an average 5 mgm Glybenclamide is equivalent to 270 mgm Chlorpropamide

TOLERANCE

Three patients on Chlorpropamide complained of general sense of uneasiness and heaviness of head. Patients on glybenclamide had no side effects.

Conclusion

Glybenclamide has been found to be remarkably powerful on weight basis being 45 times as potent as chloropamide in the present series. This does not necessarily mean that it is more effective in the treatment of Diabetes Mellitus. Actually in the present series, it has been found to be approximately equal to chlorpropamide in its ability to control Diabetes, tablet for tablet (i.e. 250 mgm of Chlorpropamide 5 mgm). The slightly better result seen with Chlorpropamide is not statistically significant. The very small dose of Glybenclamide required for control however seems to be an advantage as it has been better tolerated by the patients and there has been no side and effects in this small series so far. Glybenclamide is thus a valuable addition to our armamentarium of oral antidiabetic preparations.

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