

THE USE OF PHENMETRAZINE HYDROCHLORIDE (PRELUDIN) IN THE OBESE DIABETIC

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PRELUDIN (phenmetrazine hydrochloride) is a recently discovered agent employed in the treatment of obesity. Numerous reports have attested its value in weight reduction.¹⁻³ It has sympathomimetic properties closely allied to those of ephedrine and amphetamine, and acts as an anorexic agent but with minimal side effects on the central nervous and cardiovascular systems.

The problem of weight reduction in the obese diabetic is a difficult one. We were interested not only in the weight-reducing qualities of this agent but also in its effect on the diabetic state, particularly with respect to the blood glucose level and insulin requirements.

MATERIALS AND METHODS

Thirty obese patients with proven diabetes mellitus attending the diabetic clinic of the Royal Victoria Hospital were selected at random. The patients' ages ranged from 41 to 81 years. Fifteen of the group required daily insulin at levels varying from 16 to 60 units of protamine zinc insulin. In the remainder the diabetes was controlled by diet alone although they continued to be overweight. The weight of these patients, all overweight, had either remained stationary or was slowly increasing before the study.

The patients were maintained on their previous diabetic diets, and the dosage of insulin in those receiving it was continued at the same level throughout the course of the study. The groups were followed up for periods varying from two to six months. Reduction of the obesity was attempted by the double blind method, using either the active agent phenmetrazine hydrochloride or a matched placebo. These drugs were alternated at monthly intervals, the patient taking either 25 mg. of phenmetrazine hydrochloride or an inert placebo identical in appearance in pill form three times a day 15 minutes before meals. The weight was recorded frequently. The postcibal (P.C.) blood sugar level was determined from one to three hours after the morning meal by the method of Folin.⁴ The insulin was self-administered subcutaneously a few minutes before breakfast.

RESULTS

Ten of the 30 patients originally selected were not continued on the study because of their failure to co-operate.

It was noted that 15 of the remaining 20 patients showed a substantial degree of weight loss while

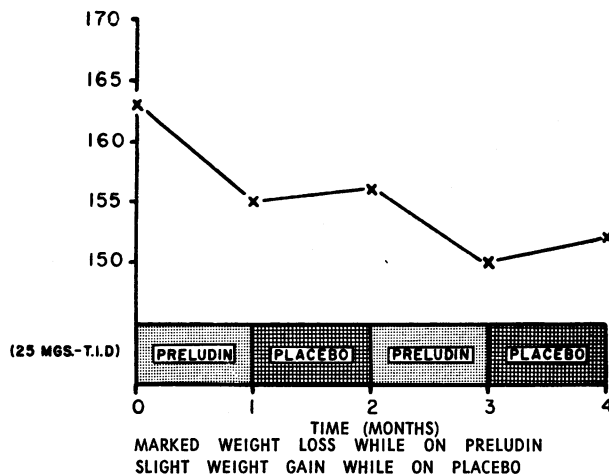


Fig. 1.—Weight loss while patient was taking phenmetrazine hydrochloride (Preludin) during two separate one-month periods is demonstrated. There was an actual gain in weight when the patient took the placebo.

taking phenmetrazine hydrochloride. It was also quite obvious that no weight was lost during the periods when the placebo was taken. In many of the patients an actual rise in weight was recorded during the placebo administration, after a previous satisfactory fall in weight had been achieved by the use of phenmetrazine hydrochloride (Fig. 1). Five patients failed to show evidence of weight loss while on the phenmetrazine hydrochloride or the placebo. On the other hand, the weight loss achieved in the successful group was of significance (Fig. 1(a)).

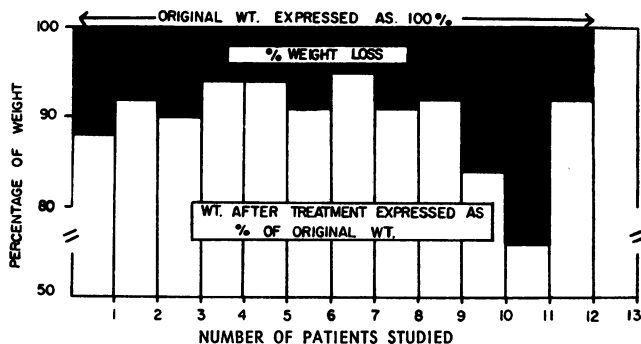


Fig. 1(a).—This figure demonstrates the weight loss in 12 patients. The original weight is expressed as 100%. The black shaded areas are the actual loss expressed as percentage of original weight.

The P.C. blood sugar level was not significantly altered by these agents. The levels in the group not taking insulin remained approximately the same while taking either the phenmetrazine hydrochloride or the placebo and compared well with those levels noted before treatment. Of the group taking insulin, those with the more severe diabetes showed a much wider range in their blood sugar levels before the study than did the non-insulin group. The wide fluctuation persisted during the study but was not intensified by either phenmetrazine hydrochloride or the placebo. Only one patient showed a definite hyperglycemic effect which might have been attributable to the phenmetrazine hydrochloride. The blood sugar levels in this pa-

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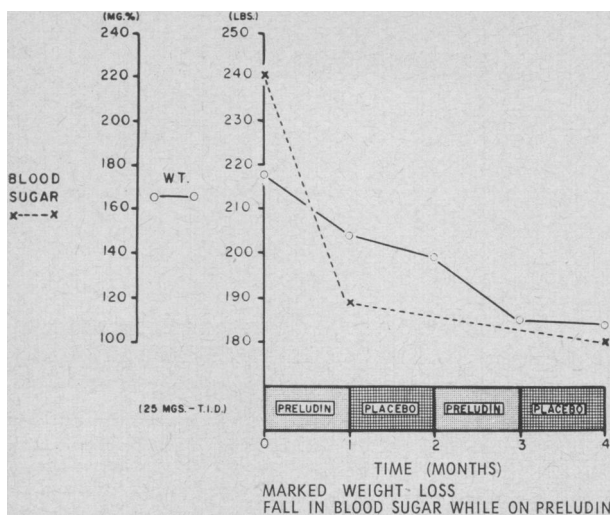


Fig. 2.—Weight loss occurred in an obese diabetic woman. The rate of loss was more marked with phenmetrazine hydrochloride than with the placebo. The P.C. blood sugar level fell rapidly concomitantly with the weight loss. Phenmetrazine hydrochloride did not cause hyperglycemia.

tient were higher during several different periods of phenmetrazine hydrochloride ingestion than before treatment or during placebo ingestion.

Blood sugar levels might be expected to fall as weight reduction occurred. This was not always the case. Only five patients had constant lowering in blood sugar levels with lowering of the weight while taking the medication. In the others, the blood sugar levels were of a similar order before and after the weight loss and whether phenmetrazine hydrochloride or the placebo was being taken. One new diabetic was treated by diet plus the above medication without the use of insulin. The blood sugar level rapidly fell to normal as the weight decreased and the normal levels persisted while the patient received the medication (Fig. 2). In most patients, however, there was little difference between blood sugar levels before treatment and during the period of study.

DISCUSSION

The treatment of obesity is notoriously difficult. Many forms of treatment including diet and medication have been used. Patients will often lose weight satisfactorily for a time, only to regain it at a later date.⁵ In others, it is often difficult to maintain weight loss for even a few weeks. The diabetic patients of our group, in most cases, had been followed up for some time without satisfactory weight reduction. Phenmetrazine hydrochloride in the dosage described was apparently of value in inducing a weight loss in two-thirds of the group. Furthermore, this did not significantly interfere with the blood sugar levels or insulin requirements. Only one patient appeared to obtain a hyperglycemic effect from the administration of phenmetrazine hydrochloride, while the others did not show an appreciable rise in blood sugar levels. However, only five patients definitely demonstrated a fall in blood sugar levels with weight loss. We

feel from this evidence that phenmetrazine hydrochloride has little or no effect on the blood sugar levels when used in this dosage. It would appear that phenmetrazine hydrochloride, together with dietary management and insulin, is another tool to be supplied in the long-term management of the obese diabetic.

SUMMARY

Thirty obese diabetic patients were followed up for a two- to six-month period during which therapy consisted of regular dietary control and insulin when indicated, together with phenmetrazine hydrochloride (Preludin) or an identical placebo.

Weight was reduced in 15 of the 30 patients.

Blood glucose levels or insulin requirements were not significantly altered by this form of therapy.

We wish to thank Geigy Pharmaceuticals for the supplies of Preludin.

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RÉSUMÉ

Les auteurs ont ajouté de l'hydro-oxazine (Préludine, marque déposée) au régime alimentaire et à l'insuline d'une série de 30 diabétiques au cours d'une période variant de deux à six mois. Quinze d'entre eux réussirent à maigrir à l'aide de l'hydro-oxazine alors qu'ils engraisserent lorsque le médicament leur fut retiré. Ce traitement n'eut aucun retentissement sur la glycémie et les besoins d'insuline.

LUNG ABSCESS COMPLICATING HEALED OPEN TUBERCULOUS CAVITY

A healed open tuberculous cavity in a young Negro male was complicated by pneumonia and a lung abscess, which did not reactivate the pulmonary tuberculosis. An acute episode of caseous tuberculous pneumonia, involving the complete left lung in May 1952, responded to one gram of streptomycin twice weekly and PAS and isoniazid in the usual dosage over a period of 9 to 13 months. A large residual cavity appeared in the left apex. Sputum was negative for tubercle bacilli on smear and culture from January 1953, and the patient was well until August 1955, when he developed an acute pneumonia with giant left apical cavity. Despite copious expectoration of sputum, no signs of reactivation of tuberculosis were found. The response to oxytetracycline was dramatic, and within a week the patient was asymptomatic, and the radiograph had returned to its previous state. It is suggested that open healing had occurred without closure of the cavity. Although this area was under constant threat of reactivation, a clear-cut episode of pneumonia produced a large cavity in the upper lobe, presumably a lung abscess, without reactivating the pulmonary tuberculosis.

It is expected that this type of complication will occur more frequently as more patients with pulmonary tuberculosis are treated at home rather than in sanatoria.—L. Breslaw: *Ann. Int. Med.*, 48: 1373, 1958.