A Hypocaloric High-Protein Diet as Primary Therapy for Adults with Obesity-related Diabetes: Effective Long-Term Use in a Community Hospital

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The use of reducing diets as the sole therapy for the long-term management of obese diabetic patients has been generally unsuccessful. Most previous attempts took place with a few patients in university hospital clinical research centers. We placed 36 such patients on a hypocaloric high-protein food diet, consisting of 1.7–2.0 g protein/kg ideal body wt, during admission to a community hospital. After beginning this diet, patients could be weaned from sliding-scale regular insulin in an average of 1.9 days. Patients remained on this diet after discharge (mean hospital stay = 4.3 days), and complex carbohydrates were gradually added up to 80 g daily. Outpatient long-term management consisted of alternating biweekly visits to a sole nurse practitioner or physician or to a group discussion meeting. Follow-up averaged 41 wk, during which eight patients (22%) had sustained weight loss throughout and remained euglycemic. Twenty patients (56%) initially lost weight (average: 23% of ideal body weight), then plateaued weight, but have also remained euglycemic. Only eight patients (22%) required insulin. Side effects of the diet were not serious in any patient; no one had myocardial irritability or serum potassium < 2.9 meq/L. This hypocaloric high-protein diet thus appears to be a generally successful means of weaning obese diabetic adult patients from insulin. This can be done rapidly, safely, and permanently in the community. Such diet therapy appears to require minimal laboratory and hospital resources that are available to all health care providers. DIABETES CARE 6: 328–333, JULY–AUGUST 1983.

The management of the obese adult diabetic patient is a common therapeutic challenge. Studies in recent years have indicated that obesity is characteristically accompanied by insulin resistance, with manifestations ranging from mild hyperinsulinemia to clinical diabetes mellitus.[1–7] Weight reduction is usually viewed as an unattainable objective for most patients.[8,9] In this setting, traditional medical treatment of hyperglycemia per se is unsatisfying. Oral hypoglycemic agents are not without side effects.[10] Likewise, there has been debate whether their use may increase the already considerable risk of cardiovascular disease in obese patients.[10,11] Furthermore, the use of either oral hypoglycemic agents or exogenous insulin contributes to the maintenance of obesity and diabetes.

Recently, a severely hypocaloric high-quality protein diet containing 1.3 g of protein/kg ideal body wt, a so-called "protein sparing modified fast," was fed to a small group of insulin-requiring obese adults in a clinical research unit.[12] All seven patients were withdrawn successfully from insulin, and had significant improvements in blood pressure, glucose tolerance, and lipid profile. The three patients who were studied maintained positive nitrogen balance. However, other investigators demonstrated equal degrees of nitrogen balance with the use of either a low-calorie pure protein diet or an isocaloric mixed diet.[13] The pure protein diet, however, resulted in mild sodium depletion, decreased sympathetic nervous system activity, and orthostatic hypotension.[13,14]

We studied the use of primary dietary therapy in obese adult diabetic patients, many of whom had been chronically treated with oral hypoglycemics or insulin. In order to increase long-term patient compliance, we liberalized the "protein sparing modified fast" to approximately 2.0 g of protein/kg ideal body wt. We report the successful long-term use of this semistarvation diet as a primary treatment for these patients, all of whom tolerated the diet without serious side effects. This study was performed in a community hospital setting without specific research facilities. Patients were followed only by a single internist and a nurse practitioner.

METHODS

Thirty-six obese (at least 20% above ideal body weight)[15] adult patients were studied after informed consent. A history of diabetic ketoacidosis was disqualifying as was any intercurrent acute illness thought to be responsible for the presenting glucose intolerance. All patients were admitted to Kimbrough Army Community Hospital. Physical examinations and routine laboratory and radiologic screening were performed. This screen consisted of a complete blood count with white blood cell differential, urinalysis, and fasting serum values for glucose, urea nitrogen, creatinine, uric acid, sodium, potassium, chloride, bicarbonate, total protein, calcium, phosphate, alkaline phosphatase, aspartate amino transferase, total bilirubin, creatinine phosphokinase, cholesterol, and triglyceride. Furthermore, a chest radiograph, electrocardiogram, and a 24-h urine for creatinine and uric acid were obtained.

All patients were begun on a modified version of the "protein sparing modified fast"[8] at admission. This diet consisted of 3.5 g of high-quality animal protein foods (equivalent to 1.7–2.0 g protein) per kilogram of ideal body weight. This was calculated (in pounds) for men as 106 + 6 × (height in inches above 60 in) and for women as 105 + 5 × (height in inches above 60 in). No carbohydrates were consumed and fat intake was calculated to be approximately 18% of total calories. Low-calorie beverages were consumed in a quantity greater than 1 L/day, and all patients were begun on a multivitamin preparation (Stuart Prenatal vitamins, Stuart Pharmaceuticals, Wilmington, Delaware). All patients were counseled by a dietitian regarding home preparation of this diet, usually in the presence of the person responsible for food preparation.

At this time any routine insulin or oral hypoglycemic therapy was discontinued. All patients were begun on a "sliding scale" insulin protocol, based on serum glucose and utilizing subcutaneous regular insulin, before each meal and at 9 p.m. Patients received 5 U for a serum glucose over 250 mg/dl, 8 U for a serum glucose over 300 mg/dl, and 10 U for a serum glucose over 350 mg/dl. Additional insulin was individually prescribed for serum glucose over 400 mg/dl. All urine was tested for glucose and acetone using Clinitest and Acetest tablets (Ames Division, Miles Laboratories, Elkhart, Indiana). An attempt was made to establish a reliable renal threshold for glucose in each patient, and to then administer the sliding-scale insulin based on urinary values.

Patients were discharged 48 h after their last insulin dose. At discharge, they were once again counseled regarding food preparation and also instructed to continue urine monitoring for both glucose and acetone. Furthermore, they were told explicitly to notify their physician (J.D.F.) or nurse clinician (E.M.S.) immediately of any problem or if their urine measurements indicated increased glucosuria.

Patients were then seen biweekly. They came to the Medical Clinic for monthly visits with either the physician or nurse clinician and on alternative visits for group sessions conducted by the nurse clinician. The latter were behavioral and supportive in nature. At each individual appointment, patient compliance was assessed by evaluating weight and fasting serum glucose as well as by evaluating the patients' record of recent urinary glucose and acetone. Additionally, the other serum analyses previously mentioned were repeated monthly, and 24-h urine samples for uric acid and creatinine were obtained after 2 mo of diet therapy.

The diet was continued without modification following discharge. After 1 mo, if patients had demonstrable and continuing weight loss, 20 g of carbohydrate was added. When patients were within 20% of ideal body weight, the diet was further augmented with a total daily intake of 80 g of carbohydrate. Upon reaching ideal body weight, the patient was placed on an appropriate American Diabetes Association diet. Liberalization of the diet was usually accompanied by reversion of urinary ketones to negative. A return to the basic protein diet was recommended when any weight gain was noted, especially if this was accompanied by a worsening of glucose control. Insulin was restarted only if patients demonstrated outpatient fasting serum glucose levels over 250 mg/dl on two successive biweekly visits. Statistical determinations were performed using nonpaired Student's *t* test or chi square analysis.

RESULTS

Patient characteristics. At the time of admission the mean age of outpatients was 52 yr; the mean weight was 156% of ideal body weight (Table 1). Nineteen of the patients (53%) were men, 22 (61%) were white. Twenty-two patients (61%) were on chronic insulin administration, 4 (11%) took oral hypoglycemics, and 10 (28%) were on no therapy. Twenty-three patients (64%) were admitted on an emergency basis, due to marked hyperglycemia, of whom 18 were injecting insulin and 3 were consuming oral hypoglycemics. Of the 13 patients (36%) with elective admissions, 4 were injecting insulin and 1 was consuming an oral agent. There were no statistically significant differences in age, weight, or initial fasting serum glucose between the groups of patients on insulin, oral agents, or diet management alone. Similarly, no

TABLE 1
Initial characteristics of study group

Age	52.4 yr (± 1.6) (SEM)	
Weight	156.4% ideal body wt (± 4.4)	
Sex	53% (19/36) men, 47% (17/36) women	
Emergency admissions	23/36	(64%)
On insulin	18/23	(78%)
On oral agents	3/23	(13%)
On diet only	2/23	(9%)
Elective admissions	13/36	(36%)
On insulin	4/13	(31%)
On oral agents	1/13	(7%)
On diet only	8/13	(62%)

significant differences in age, sex, or weight existed at the onset between those patients admitted on an emergency basis and those admitted electively.

Inpatient results. No episodes of either ketoacidosis or hyperglycemia occurred upon discontinuation of chronic hypoglycemic therapy and admission for institution of the hypocaloric diet. The sliding-scale insulin was discontinued an average of 1.9 days after admission, and all patients were weaned from insulin by the fifth hospital day. The average hospital stay was 4.3 days, during which time patients lost an average 3.5 kg (5.5% of ideal body weight) (Table 2). There were no differences among patients previously on insulin or on oral agents or those not previously treated regarding either duration of the required sliding-scale insulin administration, the length of required hospitalization, or total inpatient weight loss.

Outpatient phase. The average duration of follow-up was 41 wk. Eighty-three percent (83%) of patients were followed for greater than 26 wk. The mean weight loss for the entire group was 9.5 kg ± 1.1 (SEM). Twenty-eight patients (77%) have remained off insulin.

The group of patients studied was evaluated for the two desired endpoints of sustained weight loss and freedom from hypoglycemic medication (Table 3). Eight patients (group A) had both a sustained weight loss throughout the study and sustained freedom from hypoglycemic therapy. Twenty patients (group B) did not have sustained weight loss, but remained free of insulin requirements. Eight patients (group C) regained weight some time after discharge and could not be maintained without insulin. No patient who had a sustained weight loss required the reinstitution of insulin.

There were no statistically significant differences ($P > 0.05$) between these groups regarding characteristics at the onset of the study. There were no differences in age, sex (Table 3), fasting serum glucose, cholesterol, triglycerides (Table 4), or previous insulin or oral hypoglycemic dose. Duration of follow-up has been similar in all groups (Table 3).

Within 1 mo of beginning diet therapy, those patients who were successfully continued without insulin (groups A and B) showed significant declines in fasting triglycerides as well as in fasting glucose (Table 4). Interestingly, those patients who eventually required insulin (group C) did not, as a group, demonstrate such metabolic improvements, although no patient in this group was yet sufficiently hyperglycemic to require resumption of insulin. These differences in metabolic parameters persisted throughout the study, and comparison of final values shows a further significant decrease in mean fasting glucose and triglyceride levels into the normal range in the group A patients (who had further weight loss).

TABLE 2
Inpatient results

	Mean	Range
Duration of insulin therapy	1.9 days	0–5 days
Duration of hospitalization	4.3 days	2–12 days
Weight loss (kg)	3.5 kg	0–6.5 kg
Weight loss (% ideal body wt)	5.5%	0–13%

TABLE 3
Grouping of patients based on results of long-term diet therapy

	Group A	Group B	Group C
Number of patients	8	20	8
Sex	5M/3W	8M/12W	5M/3W
Age (yr: mean ± SEM)	55.9 ± 4.0	49.4 ± 9.1	56.5 ± 2.9
Follow-up (wk)	37.4 ± 6.2	39.2 ± 3.7	50.3 ± 4.4
Total weight loss (kg)	15.9 ± 2.1*	7.4 ± 1.2	8.0 ± 2.5
% IBW	25.4 ± 5.2*	11.8 ± 1.5	10.6 ± 3.4

Study patients were retrospectively divided among groups based on weight loss and glucose tolerance. Group A: ongoing weight loss, improved glucose homeostasis. Group B: plateaued weight, improved glucose homeostasis. Group C: plateaued weight, hyperglycemia.
*$P < 0.05$ versus corresponding values for group B and group C.

Figure 1 shows the progression of weight measurements in these groups of patients. Group B patients (without sustained weight loss but who remained insulin-free) weighed significantly more ($P < 0.05$) at the outset than those in either group. Thus, at the beginning group C patients (who later resumed insulin due to hyperglycemia) had similar mean weight to group A patients (those who lost weight and remained insulin-free). By definition, group A had a greater weight loss than the other patients; this reached statistical significance by month 2. Despite the slower weight loss by groups B and C, these patients did continue their decreases in mean weight for the first 4–5 mo. Although we did not take detailed diet histories at each follow-up visit, it appears likely that dietary indiscretion increased after that time in both groups of patients. On the other hand, after admission to

TABLE 4
Mean (± SEM) fasting glucose, triglyceride, and cholesterol values before and during long-term diet therapy

	Group A (N = 8)	Group B (N = 20)	Group C (N = 8)
Fasting glucose (mg/dl)			
Before diet	310 ± 22	307 ± 22	277 ± 30
1 mo	128 ± 26*,†	141 ± 12*,†	235 ± 31
Final	135 ± 18*,†,‡	185 ± 15*,†	290 ± 18
Fasting triglycerides (mg/dl)			
Before diet	299 ± 17	279 ± 48	286 ± 41
1 mo	125 ± 26*,†	158 ± 19*,†	282 ± 98
Final	87 ± 20*,†,‡	180 ± 23*,†	275 ± 90
Total cholesterol (mg/dl)			
Before diet	246 ± 20	252 ± 19	270 ± 33
1 mo	209 ± 43	224 ± 12	263 ± 29
Final	201 ± 14	231 ± 10	253 ± 15

Study patients were retrospectively divided among groups as described in Table 3. *$P < 0.05$ versus values before diet. ‡$P < 0.05$ versus corresponding values for group B. †$P < 0.05$ versus corresponding values for group C.

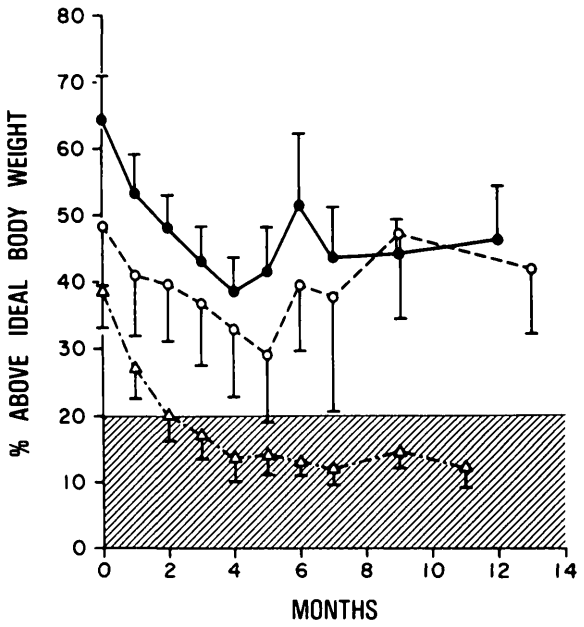

FIG. 1. Follow-up patients after institution of the hypocaloric high-protein diet. Groups are described in the text. Group A (continued weight loss, insulin-free) is denoted by △; group B (plateaued weight, insulin-free) by ●; and group C (plateaued weight, resumed insulin) by ○. After 7 mo of follow-up, some patients did not report for monthly weighing; results are thus shown for months in which half or more of the group was measured. Details of statistical significance are given in the text.

the study, there was no statistical difference at any follow-up point between the mean weights of patients in group B (who remained insulin-free) and group C (whose eventual hyperglycemia required reinstitution of insulin). Thus, although the patients in group C showed little improvement in glucose control after 1 mo of diet therapy, this group had a similar mean weight loss to the other groups.

Ten patients had never taken insulin or oral agents before admission to the study. They all maintained normoglycemia throughout follow-up (mean: 39 wk) and were thus able to avoid the institution of insulin therapy. However, 8 of 26 patients (31%) on insulin or oral agents before admission eventually became hyperglycemic and required insulin.

Side effects. Minor side effects were frequent (Table 5). The most commonly noted were muscle and joint discomfort and a change in bowel habits. One of three (33%) premenopausal women had oligomenhorrhea, which spontaneously resolved. No serum electrolyte, calcium, phosphate, uric acid, renal, or liver function abnormalities were noted in follow-up. Five patients had persistent new elevations in serum creatinine phosphokinase (CPK), in all cases of the MM band. One patient, who had an accompanying elevation in serum aldolase, underwent muscle biopsy, which showed fatty infiltration and increased muscle fiber turnover without inflammatory changes. This patient's elevated CPK values persisted after subsequent discontinuation of the diet.

TABLE 5
Side effects (N = 36)

Joint/muscle pain	41%	Cold intolerance	24%
Fatigue	31	Dizziness	21
Constipation	48	Oligomenorrhea	33 (⅓ patients)
Diarrhea	24	Decreased libido	21
Dry skin	52	Headache	28

DISCUSSION

Most adult diabetic persons are overweight. Obesity has long been known to be associated with in vivo insulin resistance[16] and hyperinsulinemia.[17] Diminished numbers of insulin binding sites have been noted on cell surfaces in this clinical setting.[15] Decreased insulin binding with consequent decreased insulin action has also been demonstrated.[18–20]

The reversibility of insulin resistance with weight loss in obese diabetic subjects has been demonstrated by improved in vivo insulin responsiveness, decreased serum insulin levels, and normalized insulin binding.[2,3] Furthermore, parameters of glucose intolerance normalized following weight loss in a small group of patients on a balanced reducing diet.[4] In clinical practice, however, weight loss seems largely unattainable.[7,8] Most physicians, therefore, manage their patients by focusing on serum glucose levels, choosing between oral agents and insulin after failure of balanced hypocaloric dieting to control hyperglycemia.

The "protein sparing modified fast" represents one method of achieving rapid recovery of insulin sensitivity in obesity-related glucose intolerance.[12] Positive nitrogen balance was originally demonstrated[12] but has been questioned.[13] Otherwise, no serious complications have been noted. Specifically, none of the cardiac rhythm complications associated with the liquid-protein-supplement diet[21–25] have been documented. This is possibly due to the high-quality protein and adequate minerals in the foodstuffs used in this diet versus hydrolyzed casein utilized in "liquid protein" supplements.[24]

Our liberalized diet increased total protein intake from 1.3 to approximately 2.0 g/kg ideal body wt, which resulted in an intake of 800–1000 kcal/day. This was all in the form of lean meat, fish, or poultry. The liberalized intake was chosen in an attempt to ensure positive nitrogen balance. We hoped also to foster better compliance by having patients weigh cooked foods. The basic protein diet was ketogenic, as assessed by urinary ketone analysis. Thus, patients could measure their own compliance, which seems important for ongoing motivation and continued correction of dietary habits.

We demonstrated that control of serum glucose can be rapidly achieved by institution of the diet in the inpatient setting in a brief hospitalization with minimal weight loss. This was possible in a small community hospital without the sophisticated laboratory support or close metabolic supervision found in most university clinical research centers. Long-term follow-up was conducted by a physician and nurse practitioner in an outpatient clinic. Limited resources in our community hospital did not allow nitrogen balance studies.

Likewise, we chose not to monitor glycosylated hemoglobin levels routinely in our patients. This determination was unavailable locally and would have required the expensive use of a reference laboratory.

We also demonstrated that, while long-term substantial and progressive weight reduction was achieved by only a minority of patients (8/36 patients, 22%), the majority (28/36 patients, 78%) could be managed without hypoglycemic agents despite minimal weight loss. Nevertheless, ongoing weight loss was not a prerequisite for insulin independence, nor did early weight loss result in good control of hyperglycemia in all patients. It is our impression that many of our patients had a crucial body weight and/or amount of carbohydrate in their diet below which they had good glucose homeostasis. Small increments above this may significantly and rapidly worsen control, perhaps due to alterations in the number of available insulin receptor sites.[18–20]

All patients who had not been previously treated at the time of admission (regardless of whether they were admitted electively or for an emergency) were able to remain off insulin in long-term follow-up. It is unclear whether these patients had less severe disease or whether psychological factors related to the possibility of insulin therapy provided sufficient motivation to adhere to the diet. The success of this program for these individuals, however, suggests that initial counseling and diet therapy for the obese patient with newly diagnosed glucose intolerance may be critical for future management.

This study reemphasizes an additional biochemical benefit (other than improved glucose metabolism) resulting from weight reduction in the obese. We found significantly improved fasting triglyceride levels in those patients achieving substantial weight loss.

Clinically important side effects were absent. Myalgias, arthralgias, and other distressing side effects have been attributed (often without objective proof) to the ketotic state.[25] Our patients did complain of arthralgias and fatigue, usually mild and transitory, in the early phases of the diet. These symptoms generally cleared, although urine ketones remained present. Altered bowel habits, perhaps attributable to the altered fiber content of the diet, were easily corrected by the addition of fiber and of stool softeners. The elevated CPK values, apparently from peripheral muscle, are of unknown significance. Nevertheless, a specific diet-related myopathic process is quite unlikely. Likewise, neither hypokalemia nor myocardial irritability (both seen with liquid protein diets) were noted in any of our patients.

Thus, diet therapy of the obese diabetic patient is an achievable goal in most cases. This study was conducted in a small community hospital by a few health professionals. The setting was quite similar to that of most community-based internists and family physicians and demonstrates that local resources are sufficient to conduct such therapy. Routine medical and laboratory facilities provided all support needed, and at minimal cost. Such therapy, however, does require considerable perseverance by patients and physicians. Enthusiastic and frequent support by health care professionals may be the key to long-term success.

Note added in proof. We have continued this study since the submission of this manuscript. Of the original 36 patients, eight have been lost to follow-up. The remaining 28 patients have been followed an average of 91 wk; 18 of them have been followed for more than 2 yr. Thirteen patients (46%) remain on diet alone (one is losing weight and 12 have plateaued weight). Five patients (18%) are presently treated with oral hypoglycemic agents and 10 patients (36%) are on insulin therapy. Seven of the 10 patients who were euglycemic on diet alone after 1 yr have remained so for a further year.

We have more recently enrolled another 17 patients. They have been followed an average of 16 wk (five patients have been followed more than 26 wk). Again, insulin could be rapidly withdrawn (in an average of 1.1 days), and hospitalization was brief (averaging 4.4 days). Eighty-two percent of these patients have had sustained weight loss (averaging 11% of ideal body weight), while 18% have plateaued. None has resumed insulin or an oral agent. To date, none of our patients has had any serious myocardial or electrical abnormalities or discontinued the diet due to side effects.

The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

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