The Effects of Anxiety Management Training on the Control of Juvenile Diabetes Mellitus

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The present study was designed to determine whether diabetic control could be improved through the direct psychological management of stress and anxiety. Five poorly controlled female adolescent diabetics ranging in age from 15 to 18 years were used as subjects. All were seen on an outpatient basis over a 6-month period. A single-subject format employing a multiple-baseline design across subjects was used. The independent variable used was a technique known as anxiety management training. Baseline, attention-control, and treatment data were collected on a number of dependent measures. Subjective estimates of anxiety and tension by each subject were gathered on a biweekly basis using the Multifactorial Scale of Anxiety. Diabetic control was assessed daily using the Diastix method and weekly using the 24-hr quantitative glucose method. Data on the five subjects suggested that improved control of stress and anxiety had a positive effect on diabetic regulation. Lower and more stable urine glucose levels using both urine testing methods were found. However, no decreases in the subjects' personal assessment of tension and anxiety were evident.

KEY WORDS: juvenile diabetes; anxiety management training; diabetic control; stress management.

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INTRODUCTION

Since the earliest description of diabetes mellitus there has been much speculation regarding the relationship between emotional factors and the disease. Numerous studies have documented that in many individuals events of a psychological nature may act as precipitating agents in altering the course and control of the disease leading to poor diabetic stability (Hinkle and Wolf, 1952a, b; Hinkle *et al.*, 1951a, b, 1959a, b; Vandenbergh *et al.*, 1966, 1967). These studies indicate that blood glucose values can be either increased or decreased by stress.

However, some of this research indicated that in younger insulindependent diabetics, stress led to an increase in glucose values. This finding closely parallels the clinical observation that juvenile diabetics are likely to be in poor control when under stress. The issue of diabetic instability is of particular concern in children since poor metabolic regulation has been found to be associated with a number of immediate and long term complications. In the short term states of mild to severe hypoglycemia and hyperglycemia are encountered. In the long-standing juvenile diabetic, vascular, ocular, renal, and neuropathological disease is often seen where control has been difficult. Concomitant with the physical complications are psychological factors which interfere with the child's social, emotional, and academic development (Fallstrom, 1974; Koski, 1969; Galatzer *et al.*, 1977). Hospitalization and/or periods of illness inevitably interfere with all facets of biological as well as psychosocial development.

Few attempts of an empirical nature have been made to improve the course and control of juvenile diabetes through psychological intervention procedures (Johnson, 1980). A study by Minuchin and Barcai (1969) found family psychotherapy to be effective in reducing the emotional lability of a diabetic child leading to better diabetic control. However, the lack of follow-up data and the paucity of subsequent studies of this nature preclude inferences from being made regarding its usefulness. A more recent report by Fowler *et al.* (1976) has shown that electromyograph biofeedback relaxation training resulted in a decreased level of insulin intake in a 20-year-old diabetic woman. A similar approach using seven subjects was reported in an abstract by Guthrie *et al.* (1976). However, neither of these studies was well controlled and methodological problems restricted the generalizability of the findings.

Since the literature suggests a strong association between emotional lability and inappropriate metabolic regulation in juvenile diabetics, it would seem important to investigate whether diabetic control could be enhanced if patients were taught to reduce the effects of emotional factors on physiological functioning.

In the past few years several relaxation training techniques have been employed in the treatment of stress-related disorders such as tension headache (Cox *et al.*, 1975), hypertension (Shoemaker and Tasto, 1974), and insomnia (Nicassio and Bootzin, 1974). Anxiety management training (AMT) (Suinn, 1975) has been of demonstrable value in individuals who suffer from general anxiety and stress where the reduction of specific and nonspecific tension is desired.

The present study was designed to assess the efficacy of AMT with juvenile diabetics. It was hypothesized that AMT would provide these children with a procedure in which some control over emotional stress could be maintained. This reduction in stress would lead to a subsequent improvement in metabolic control as demonstrated by reduced and more stable glucose levels. In addition, it was hypothesized that a reduction in subjectively experienced levels of anxiety would be found.

METHOD

Subjects

Thirty-six poorly controlled adolescent diabetics selected from the Diabetic Clinic of the Children's Hospital of Eastern Ontario (CHEO) were contacted by telephone regarding possible participation in the study. Of these, 30 declined to participate because of the time factor involved, disinterest in the study or illness. As a result, six female subjects between 15 and 18 years of age were included in the study. Data on only five of these six subjects could be subjected to analysis, however, as one of the subjects became so labile in her control during the study that frequent hospitalization and insulin adjustments made her test results uninterpretable.

All subjects who agreed to participate in the study were seen in a 20- to 30-min clinical interview. The main purpose of the interview was to describe the study in detail and to establish whether the subject had an anxiety or tension problem that possibly interfered with good diabetic control. Other information gathered centered around the chronicity of the problem and the physical symptoms associated with anxiety and tension. It was also determined to what extent, if any, the individual attempted to rectify the problem through either psychotherapy, medication other than insulin, or other means.

No subjects exhibited evidence of serious medical disorders which interfered with their participation in the study. All subjects had been diabetic for at least 3 years, with the mean age of onset being 9 years. All subjects lived at home with at least one parent. Both the children and their parents were informed as to the exact nature of the study and the techniques to be employed before consent forms were signed.

Setting

All children involved in the study were seen on an outpatient basis in the Diabetic Clinic of CHEO. The study was conducted over a 150-day period. Urine samples of the subjects were analyzed in the laboratories of CHEO without the technician knowing the treatment stage of the child.

Treatment Procedure

A single-subject format employing a multiple-baseline design across subjects was used. This design was chosen because of the irreversibility and carryover effect of the therapeutic instructions in adjacent phases. Variable time periods for each subject in each phase were selected to ensure adequate data collection and to reduce the chance that environmental factors might affect the treatment outcome.

Following the baseline phase ranging from 21 days for subject A to 54 days for subject E, an attention-control (A-C) condition ranging from a predetermined length of 14 to 29 days was instituted. The use of the attention-control condition strengthened the design by allowing the effects of the independent variable to be compared to both baseline and attention-control phases.

The A-C condition consisted of psychological testing utilizing the Minnesota Multiphasic Personality Inventory (Hathaway and McKinley, 1967) and the Wechsler Intelligence Scale for Children – Revised (Wechsler, 1974) or the Wechsler Adult Intelligence Scale (Wechsler, 1955). Each subject was given a treatment rationale which explained that often a knowledge of one's psychological makeup is of benefit in coping with daily life experiences and may serve to bring about better diabetic control. All testing and feedback were performed within a 7-hr period over 2 weeks so as to be as equivalent as possible to the actual treatment time. The context of the feedback sessions was kept as neutral as possible so that as little biasing as possible would be introduced.

Institution of the AMT condition was implemented following each subject's attention-control phase. This consisted of 7 hr of anxiety management training taught over a 2-week period at the beginning of the phase. After the 7 hr of training, each subject was given a cassette tape with

muscle relaxation instructions recorded on it. Subjects were requested to practice relaxation with the tape at least three times per week and were also requested to use the relaxation skill whenever they faced stressful situations over the course of the condition. No data were collected on the subjects' compliance to this request, however. The length of this phase ranged from 71 to 115 days. Table I indicates the exact number of days the subjects spent in each phase.

Assessment Instruments

A five-item, 10-point credibility/expectancy for improvement scale similar to that used by Borkovec and Nau (1972) was administered to each subject before and after the A-C and treatment phases to measure nonspecific treatment factors such as patient expectancy for therapeutic gain and perceived treatment efficacy, as well as to gain control over experimenter-subject contact.

Subjective estimates of anxiety and tension were gained through the use of the Multifactorial Scale of Anxiety (Fenz and Epstein, 1965), where each subject was asked to respond to each item according to recent subjective feelings. This scale was administered on a biweekly basis. The Multifactorial Scale of Anxiety consists of a total of 53 items, comprising three subscales measuring state anxiety: Muscle Tension (MT; 18 items), Autonomic Arousal (AA; 16 items), and Feelings of Insecurity (FI; 19 items). The Muscle Tension subscale contains items describing the effects of sustained contraction of striated muscles such as tremor, motor incoordination, backache, neckache, rapid breathing, tension headaches, and skin sensitivity. The Autonomic Arousal subscale contains items referring to visceral symptoms relative to activation of the autonomic nervous system such as tachycardia, vasomotor reactions, emotionally induced sweating, failure of body temperature control, and digestive disorders. The Feelings of Insecurity subscale contains items referring to subjective states of fear and insecurity and concomitant behavior and attitudes such as the

Table I. Number of Days Spent inEach Phase						
	Phase					
Subject	Baseline	A-C	AMT			
Α	21	14	115			
В	32	29	89			
С	39	22	89			
D	47	14	89			
E	54	25	71			

inability to relax and concentrate, the tendency to worry over small matters, unexplained feelings of fear and panic, fitful sleep, and compulsive mannerisms. Reliability coefficients obtained from a sample of male and female university students (Fenz and Epstein, 1965), corrected for attenuation, for the scales MT, AA, and FI were 0.84, 0.83, and 0.85, respectively.

Degrees of diabetic control were assessed through the use of physiological tests. Urine testing performed at home on a thrice daily basis served as the cornerstone of diabetic assessment using the Diastix method (Ames Co. Ltd., Elkhart, Ind.). Urine tests were performed in the morning, in the late afternoon, and at bedtime and an average reading was then calculated for the day. The children entered their test results as well as their insulin intake in a diabetic diary. Test results read negative, trace, $\frac{1}{4}$, $\frac{1}{2}$, 1, and 2% which referred to the quantity of glucose in the urine. Information relating to caloric intake, exercise, medication, infection, accidents, and emotional conflicts were also entered in the diary. Insulin intake was kept constant throughout the study for each subject. The frequency of insulin injections and type used was kept as equitable as possible across subjects. Each subject's height and weight were measured both before and after the study in an attempt to ascertain dietary compliance.

In addition, assessment of urine glucose homeostasis was also determined on a weekly basis using the 24-hr fractional quantitative glucose method (Forman *et al.*, 1974). Urine voided during the day and night was collected and was kept refrigerated or frozen until the specimens could be taken by the children's parents to the hospital laboratory and analyzed. Volumes were collected at home, aliquoted into four separate containers, and labeled with time of collection and total volume: (1) 8 AM-noon (first voided overnight urine was discarded); (2) noon-4 PM; (3) 4 PM-8 PM; and (4) 8 PM-8 AM (first voided overnight morning urine was collected). Routine urine testing for glucose, three specimens a day, continued during this time. All the urine voided, but the few drops necessary for performing the tests, was added to the collection bottle. Children were considered in good control if only 20-60 g of glucose was spilled per day in the urine.

In order to assess the subject's compliance with the experimental regimen, all parents were asked to keep a diary similar to the child's. Parents were requested to check the accuracy of their child's urine test 50% of the time as randomly chosen by the primary investigator. Reliability checks were then calculated.

RESULTS

Urine Glucose (Diastix)

As can be seen from Table II, all subjects showed mean urine glucose values of $\frac{1}{2}$ % or higher during the baseline phase. By the end of the A-C phase the mean urine glucose values had declined slightly except for subject E, whose mean urine glucose rose somewhat. By the end of the AMT phase all subjects exhibited considerable decreases in their mean urine glucose values.

The results of each subject's daily urine test results were subjected to statistical analysis through the use of the TMS (Time Series Experiments) computer program (Bower *et al.*, 1974).

For subject A (Table II) differences between the baseline and the A-C phases were not statistically significant. Differences between the baseline and the AMT phases were found to be statistically significant (t = -3.36, df 134, P < 0.01). Significant differences were also found between the A-C and the AMT phases (t = 3.90, df 127, P < 0.01). It also appeared that during the baseline and A-C phases there was more variance compared to that exhibited in the AMT phase.

For subject B differences between the baseline and the A-C phases were not statistically significant. Significant differences were found, however, between the baseline and the AMT phases (t = 4.56, df 119, P < 0.01). Variance in the A-C phase was slightly reduced from the baseline phase but was elevated in the AMT phase.

Subject C's mean urine glucose level during baseline was not statistically different from that in the A-C condition. Differences between the baseline and the AMT phases were statistically significant (t = 6.46, df

Subject	Phase					
	Bas	eline	A	A-C	A	MT
A	0.56	$(0.20)^{a}$	0.44	(0.14)	0.26	(0.10)
В	1.20	(0.41)	0.98	(0.30)	0.61	(0.33)
С	1.10	(0.33)	0.91	(0.14)	0.72	(0.20)
D	1.24	(0.41)	0.92	(0.38)	0.48	(0.26)
E	0.80	(0.24)	0.88	(0.20)	0.59	(0.26)

Table II. Mean Urine Glucose Percentages (Diastix)

"Values in parentheses indicate standard deviations.

96, P < 0.01). A significant difference was also found between the A-C and the AMT phases (t = 3.08, df 81, P < 0.01). Variances were reduced from the baseline phase in both the A-C and the AMT phases.

Nonsignificant differences between the baseline and the A-C phases were found for subject D. However, the difference between the baseline and the AMT phases was statistically significant (t = 9.04, df 125, P < 0.01), as was the difference between the A-C and the AMT phases (t = 4.43, df 95, P < 0.01). As in the previous subjects, variance in the AMT phase was reduced compared with that in the baseline condition.

Differences between the baseline and the A-C phases for subject E were not found to be statistically significant. Differences between the baseline and the AMT phases were found to be statistically significant, however (t = 4.02, df 117, P < 0.01). Significant differences were also found between the A-C and the AMT phases (t = 4.27, df 86, P < 0.01). Here, the variances were not appreciably different across phases.

Twenty-Four Hour Fractionated Urine Glucose

As can be seen from Table III, the results of the 24-hr urine glucose collection are not as consistent across subjects as the daily urine test results. This may be due in part to the frequency of missing data or the infrequent application of the tests themselves, even though done on a weekly basis for 21 weeks. In addition, the variance in test results across phases for each subject appear to fluctuate in magnitude partially due to the small number of observations across phases and partially due to the lability of the degree

Glucose Values (g/24 hr)					
Subject	Phase				
	Baseline	A-C	AMT		
A	117.2	154.0	72.8		
	$(23.4)^{a}$	(81.0)	(34.1)		
В	128.5	55.3	70.0		
	(10.6)	(15.6)	(36.1)		
С	104.9	151.2	125.3		
	(37.9)	(24.0)	(47.0)		
D	158.9	104.0	61.0		
	(82.7)	(96.1)	(35.3)		
Ε	79.7	123.2	38.2		
	(27.0)	(17.5)	(26.1)		

Table III. Mean Fractionated UrineGlucose Values (g/24 hr)

"Values in parentheses indicate standard deviations.

of diabetic control each subject exhibited. Because there were only 21 observations in all and not one phase had more than 11 observations, statistical analyses using the TMS program were unable to be performed. In addition, no other inferential statistical model could be used due to the time series nature of the design.

Table III illustrates subject A's results. During the baseline phase her urine test results showed her to be excreting a mean of 117.2 g of glucose/24 hr. This rose by 31.3% to 154 g during the A-C phase but dropped by 52.7% from the A-C phase to 72.8 g during the AMT phase.

With subject B, only two observations were gained in the baseline condition for a mean value of 128.5 g glucose/24-hr period. During the A-C condition only three observations were gained, for a mean value of 55.3 g. In the AMT phase subject B's score rose by 26.5%, to a mean value of 70.0 g averaged over nine observations.

Subject C was found to be excreting 109.9 g of glucose/24 hr during the baseline phase. This increased to 151.2 g during the A-C phase, an increase of 49.1%, but decreased to 125.3 g during the AMT phase.

Subject D's test results show a consistent decrease in the amount of glucose excreted across phases. During the baseline phase she excreted a mean of 158 g over six observations, with high variability. Within the A-C phase her mean glucose output dropped to 104 g, a decrease of 34.1%. A mean glucose level of 61 g or a decrease of 41.3% during the AMT phase, with moderate variability, tends to suggest a more consistent decreased level of glucose output.

During the baseline phase subject E produced a mean of 79.7% g of glucose/24 hr. This rose by 54.5%, to a mean of 123.2 g, during the A-C condition and dropped by 68.9%, to a mean of 38.2 g, during the AMT phase.

Multifactorial Scale of Anxiety

No significant differences were found across phases for any subject on any of the subscales.

Treatment Credibility

Both the A-C and the AMT treatments were rated as moderately to highly credible both at the beginning and at the completion of their respective phases. T tests for correlated samples between phases based on the five-item 10-point credibility/expectancy for change scale revealed no significant differences for four of the five subjects. Only one subject's differences

reached significance (t = 2.22, df = 9, P < 0.05). Observed differences in treatment outcome cannot be attributed to differences in treatment credibility for the subjects whose credibility scores were not significantly different. For the subject whose credibility scores were significantly different, the possibility exists that this could account for treatment outcome, but in light of the data from other subjects it is unlikely that this was a factor.

Reliability

On selected days chosen at random by the experimenter, reliability data for the daily urine glucose tests were obtained by either one of the child's parents. The parents were instructed to record their child's test results in a diary similar to the child's by comparing the color of the reagent strip after being dipped in the child's urine to the color chart on the Diastix package. Reliability checks were to be performed three times per day for 75 of the total 150 days that the children were in the study. Reliability was calculated by averaging the total of the subject's daily urine glucose values and those of the parent's observations, dividing these observations, and then multiplying this by 100. Reliability of test results ranged from 100 to 86.9%, with a mean of 95.4%. The parents' cooperation in carrying out the reliability checks ranged from a high of 75.3% to a low of 34.3%, with a mean of 55.6%.

Compliance with Therapeutic Regimen

Insulin levels were set at the beginning of the study and were not changed during the course of the experimental program. No formal reliability measures were taken other than the subjects noting the type, dosage, and time of injection in the daily diary. In addition, contact with the physician responsible for the care of each child indicated that no changes in insulin intake were ordered during the time the children were in the study.

Each child who participated in the study met with the hospital dietician, who specified the daily caloric intake tailored to that child's needs. Generally, caloric intake was set so that the children would maintain their present weight or lose a few kilograms. However, dietary compliance was poor in three of the five subjects. Subject C actually gained 3.2 kg, suggesting that she did not follow her diet closely. It is interesting to note that she seems to have shown one of the poorest responses insofar as her 24-hr urine glucose output was concerned, as her mean output during the AMT phase was even higher than her mean output during the

baseline phase. None of the other subjects showed as poor a response. At the other extreme, subject D, who lost 1.3 kg, showed the greatest decreases from the baseline phase to the AMT phase on both measures of urine glucose excretion.

DISCUSSION

The results of this study suggest that for children who participated, anxiety management training was indeed effective in improving the course and control of the disorder by improving metabolic regulation. All subjects displayed statistically significant and clinically valuable decreases in their daily mean urine glucose levels between baseline and AMT phases as well as between A-C and AMT phases as measured by the Diastix method.

The results of the weekly 24-hr fractionated urine glucose analyses were not as clear, although decreases in mean urine glucose levels between baseline and AMT phases were found in four of five subjects. Increased variability of glucose levels using this technique was a complicating factor which made interpretation of the results difficult. In spite of the variability of test results, it is nevertheless felt that the 24-hr urine collection may be a valid measure of assessment. Variability could certainly have stemmed from any number of sources ranging from dietary factors to changes in exercise levels or stress levels of the children. However, repeated testing over time was thought to provide an accurate reflection of routine management which was representative of the child's weekly pattern. Perhaps what is required with this technique is more prolonged testing over several months in order to demonstrate more reliable changes.

With both testing methods the A-C condition could be viewed as an extended baseline which had little therapeutic value compared to the AMT condition. With the institution of the AMT procedure, improvement in control was more evident.

Two hypotheses are felt to account for these changes. On the one hand, it may be that the subjects, having begun to self-monitor their control, made greater efforts to adhere to their therapeutic regimens. This possibility supports the contention that improved compliance to treatment regimens may lead to better metabolic control. Indeed, the effect of closer monitoring and supervison of self-care has been found to be associated with improved compliance (Haynes and Sackett, 1976). Accurate charting may therefore cause improved compliance which results in improved control. Contingency management procedures similar to that used by Lowe and Lutzker (1979) illustrate this point. If patients are able to see the beneficial effect of such programming on their levels of control, then it may provide the necessary reinforcement to continue with it. An important factor leading to poor compliance is that often patients do not see the value of treatment (Haynes and Sackett, 1976).

Conversely, it may be hypothesized that the significant reduction in glucose levels in the AMT phase occurred due to the direct influence of the relaxation procedure on psychophysiological mechanisms. Improvement in medical outcomes through stress management procedures such as AMT have been demonstrated in studies dealing with such disorders as hypertension (Bloom and Cantrell, 1978) and duodenal ulcers (Brooks and Richardson, 1980). In this study increased relaxation may have decreased metabolic lability resulting in lower urine glucose levels. It may be that muscular relaxation caused somatic–autonomic connections to reduce sympathetic activity levels leading to decreased levels of urine glucose. The results of both the Hinkle and Vandenbergh studies and the findings of the present research seem to add support to the hypothesis that stress and anxiety may have direct metabolic effects on levels of diabetic control and that stress reduction may bring about an improvement in control through physiological mechanisms.

A more likely explanation for the observed changes is that indirect and direct effects of stress and anxiety affect diabetic control. However, the paucity of relevant research prohibits strong statements supporting either hypothesis alone. As a consequence, methods of improving diabetic control must focus on reducing the destabilizing effects of stress and anxiety and fostering improved self-care in poorly controlled diabetics.

While the results of the study demonstrated that AMT had beneficial effects in generally reducing and stabilizing urine glucose levels, no such effect was found on the subjects' perceived appraisal of their personal anxiety response patterns. It would appear that the AMT treatment was more effective in decreasing the physiological effects of anxiety than the perceptual aspects. However, it may well be that reductions in perceived anxiety are not related at all to reductions in urine glucose levels. In other words, it is possible that another mechanism is at work here. During the interview period with the subjects at the beginning of the study, there was an indication that some subjects tended to repress or deny the existence of physical aspects of anxiety while still appearing tense. It could be that the patients did not have a well-developed sense of their own anxiety response patterns.

Whitehead *et al.* (1979) have posited that certain psychophysiological disorders such as hypertension, coronary heart disease, and diabetes tend to be associated with stressors of an environmental nature. While symptoms may reflect the degree of these stressors, patients may be unaware of personal anxiety responses resulting in an absence of reported symptoms.

Recent research has suggested that awareness of muscle tension relative to depths of relaxation is not highly correlated (Stilson *et al.* 1980). The accuracy of passive verbal judgments of anxiety and tension levels is often unrelated to physiological measures of anxiety. Van Egeren (1971) stressed that anxiety is a multidimensional concept which is comprised of experiential, biological, and behavioral systems. In support of this hypothesis, Lang (1971) proposed that "emotional behaviours are multiple system responses made up of verbal-cognitive, overt motor and physiological (autonomically innervated organ and tonic muscle activity) events. All systems are modulated by neural centers within the brain, but the correlations between their outputs are surprisingly low" (p. 105).

The lack of concordance between subjective and physiological measures of emotional states is not a new finding. Schachter (1964) posited that emotional states are in part defined by the ongoing physiological state and partly by the individual's cognitive appraisal of this state. It would seem likely that this fact was at least partly responsible for the findings of the present study. Several authors (Brown, 1974; Budzynski and Stovya, 1969; Meichenbaum, 1976) have suggested that a necessary factor in the ability to reduce tension levels leading to deepened relaxation is an awareness in variation of muscle tension. Whenever awareness is not adequate or accurate, congruency between the cognitive and the physiological systems may be facilitated by training.

Thus, the relationship of stress to the course and control of diabetes based on available research must be addressed with caution. Most work in this area has often failed to distinguish between the direct effects of anxiety and the result of the patient's increased attention to the management of the disease while being helped with the reduction of anxiety. The present study attempted to deal with this problem by instituting the attention control condition.

Due to the highly individualized impact of different factors on each subject, it is difficult to make blanket statements regarding treatment effects. The results of the present study have to be attenuated on the basis of several factors including the fact that the subjects were female and the number of subjects who participated in the study was very small, causing any uncontrolled (e.g., caloric intake) variables to impact on the findings. Those who did participate may not have been representative of the general population of poorly controlled adolescent diabetics. In addition, the use of urine glucose analyses alone may not be as direct a measure of the physiological effects of anxiety as more rigorously controlled laboratory methods. Nevertheless, efforts were made to investigate empirically diabetic management in the natural environment as unobtrusively as possible. Further research is needed to assess those factors which influence an individual's self management and adjustment to diabetes. More clinical and fundamental investigations are needed to better characterize and quantify how stress and anxiety affect carbohydrate metabolism in diabetic patients. Health care professionals must become aware of the factors which contribute to compliance and noncompliance in juvenile diabetics and thereby develop treatment regimens which can be incorporated into the patient's life-style. In doing so, it is hoped that answers may be gained which will facilitate improvements in the course and control of juvenile diabetes mellitus.

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