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Growth in diabetic children

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GROWTH IN DIABETIC CHILDREN

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TABLE OF CONTENTS

INTRODUCTION

Numerous studies of children with diabetes have been reported. In children who acquire diabetes at some time before cessation of growth, retardation in the growth curve is often encountered. There is no apparent agreement as to pathogenesis of this diabetic growth disturbance.

This study of 57 diabetic children was prompted by the general disagreement in findings in growth studies and by questions posed by a member of the Pediatric Department, University of Nebraska School of Medicine.

PURPOSE

The purpose of the study was to see if there was any statistical significance in the following:

1. Statistical significance of differences between weight and height of diabetic children as a group.
2. Statistical significance of differences between weight and height and severity of disease.
3. Statistical significance of differences between weight and height and age of diagnosis.
4. Statistical significance of differences between weight and height and duration of diabetes.
5. Statistical significance of differences between age of diagnosis of diabetes and severity of disease.
6. Statistical significance of differences between control, whether good, fair or poor, and severity of the disease.
7. Statistical significance of differences between control and units of insulin change during the two week period of encampment.
8. Statistical significance of differences between boys and girls with respect to units of insulin change over the two week period.

METHODOLOGY

The data for this study of 57 diabetic children was collected at Camp Floyd Rogers, Nebraska City, Nebraska, during a two week encampment of these children.

Camp Floyd Rogers, for diabetic children, was started in 1951 by Dr. F. Rogers M.D., a Nebraska physician, who felt that such a camp could serve a useful purpose.

The camp operates under the sponsorship of the Nebraska Diabetes Association and is not limited to children living in Nebraska. For those who cannot meet the financial cost of $50.00 for the two week encampment, assistance is provided through various organizations.

The camp is open to both boys and girls, eight years of age or older, who have diabetes. The upper limit on age not being definately set but is about sixteen or seventeen years. The camp can accomodate approximately 64 children.

In that there is no restriction as to being from Nebraska, with the outside financial help available, and wide range in age, this sample of 57 diabetic children does not seem to be grossly biased except for the fact that children who are extremely labile may not have attended, as parents may have wanted to keep them home. Also it may be true that some children with diabetes may not have attended because of the lack of parental concern.

A percentile rank was given each child, with respect to height and weight, using the tables arrived at by the Harvard School of Public Health on Studies of Child Health and Development (20).

Severity of disease was judged on a somewhat arbritrary basis, using units of insulin. A child was judged a mild diabetic if his required dosage was 20 units or less, moderate if dosage ranged between 21 and 40 units and severe if dosage of insulin was over 40 units. Using these criteria, 11 children (10 girls 1 boy) were classified mildly diabetic, 23 children (12 girls 11 boys) were classified moderate, and 23 children (12 girls 11 boys) were classified severe. Ratings of mild, moderate and severe were given numerical ratings of 1, 2, and 3 respectively for ease in statistical evaluation.

The criterion for control of the diabetes, data taken from the end of the two week camp, was arrived at as follows:

1. Good control if the child required less than 15 units change, ie. a difference of less than 15 units in total insulin dosage from that dosage taken when arriving at camp - the home dose.
2. Fair control: 15 to 20 units difference.
3. Poor control: over 20 units change.

No child was adjusted at any one time with more than 4 units of insulin.

Using these criteria there were 37 well controlled diabetic children, 9 were fair controlled and 11 were considered poorly controlled.

Other necessary data such as age, date of onset of diabetes, etc. was taken from camp records (physical exam) completed the first day of encampment.

TABLE I

Factors		Mean.	S.D.	tm	t	r	df
Height	%ile Ht.	48	30	1.56	.85	.71	55
Weight	%ile Wt.	56	27				
%ile Wt. & Severity	%ile Wt.	56	27			.064	112
	Severity	2.2	.71				
%ile Ht. & Severity	%ile Ht.	48	30			.085	112
	Severity	2.2	.71				
%ile Ht. & ADD	%ile Ht.	48	30			.26	112
	ADD	8.3	3.3				
%ile Wt. & ADD	%ile Wt.	56	27			.21	112
	ADD	8.3	3.3				
%ile Wt. & DD	%ile Wt.	56	27			-.14	112
	DD	3.9	2.6				
%ile Ht. & DD	%ile Ht.	48	3.0			-.19	112
	DD	3.9	2.6				
ADD & Severity	ADD	8.3	3.3			-.16	112
	Severity	2.2	.71				
DD & Severity	DD	3.9	2.6			.38	112
	Severity	2.2	.71				
CD & Severity	Control	1.5	.80			.164	112
	Severity	2.2	.71				
CD & Units Insulin	Control	11.7	7.5			.25	112
	Units	36.8	18.5				
Insulin Change	Female	12.7		1.39	.87		55
	Male	10.1					

ADD Age Diagnosis of Diabetes

DD Duration of Diabetes

CD Control of Diabetes

DISCUSSION AND CONCLUSIONS

In this study of 57 diabetic children who attended a two week summer encampment at Camp Floyd Rogers, Nebraska, the following is concluded.

1. These children were found to be slightly under the average for their age groups in height. As a group these children tended to weigh more than the average for their age groups. This observed difference in deviation from mean average weight and height values as compared to each other is statistically significant at the 1% level of confidence.
2. There was no statistical correlation between height and weight and severity of disease.
3. That even though these children had a tendency to be overweight, this was no measure of severity of the diabetic state.
4. There is a slight correlation between age of diagnosis of disease and per-centile height and weight ranks, but this correlation is not marked. This means that the older the child was at the time of diagnosis of his diabetic condition the higher the child tended to rank, at the time of the study, on per-centile height and weight scales.
5. As a group the longer the children had diabetes

mellitus, the lower they tended to rank on percentile height and weight scales. This, too, is not a marked correlation, r being -.19 and -.14 respectively.

6. The younger the child was when the diabetes was diagnosed the more severe the disease tended to be at the time of the study, according to the criteria used for severity. This is a moderate but not a marked degree of correlation, r value being .38.
7. According to the criteria for control and severity of disease used in this study, the factors showed only a minor correlation, r value being .164.
8. Boys tended to be somewhat more stable than girls with respect to change in insulin requirements during the two week period studied. Average change for boys was 10.1 units of insulin and for girls 12.7 units. This difference though quantitatively small is still significant at the 2% level of confidence.

SUMMARY

The object of this study was to determine whether or not with a given random group of diabetic children any marked differences could be noted with respect to their growth and development as compared with the national average. (The Harvard scales were used as the basis for comparison). Overall, any deviation from the average noted were not striking. Stated otherwise, it would appear that as far as these particular children are concerned their most obvious abnormality is diabetes; developmentally it would be hard to conclude that they were different from any other random group of children of the United States. To a small extent, they did tend to be slightly more heavy than the average, yet not strikingly so.

In attempting to evaluate several aspects of growth and stage or degree of disease, moderate tendencies again can be observed, but none of these seem to be so striking as to provide much insight into the characteristics of diabetes as such. According to the criteria used in the study, the most closely correlated factors turned out to be duration of the disease and its severity. Probably, this represents something of a confirmation of what the clinician might have anticipated. Even here, while this is the clearest example of definite correlation between factors to be drawn from this study, none-the-less, the correlation here is not objectively a very marked one.

It is this author's intention to further pursue the problem of growth and development as it concerns children at the Camp Floyd Rogers diabetic camp. More data will be collected this summer and it is anticipated that groups within groups will be studied, ie. comparing growth curves of girls at a certain age with boys of equivalent age, who had the onset of their disease at the same time. It is further planned to obtain the clinical records of these children and determine from these data whether or not there was a period of delayed or accelerated growth prior to the onset of diabetes, and to see whether or not this is statistically significant when compared to a national average.

It is planned to use urine sugars as a guide to the degree of control of the diabetic state, rather than changes in insulin dosage, and another attempt will be made to correlate this with severity of disease.

It is the author's plan to collect data at each Floyd Rogers encampment for the next three to four years, and each year refine the design of the basic experiment in hopes of arriving at some data that may shed light on some aspects of growth and development in diabetic children.

REVIEW OF LITERATURE

It is probably safe to assume that there was not a great deal of study about growth retardation in diabetic children during the pre-insulin era because the disease exacted its toll before any developmental changes could be noted.

In reports from the pre-insulin era, which are very few, there is evidence that those children suffering from diabetes and who were kept alive for a few years suffered a marked retardation in growth (3).

Joslin (1925) collected data for two years from 20 pre-insulin survivors and found an increase in body weight in only one person during his observation of studies. Joslin also studied 12 mildly diabetic individuals, who required no insulin for a period of 3.6 years and found that there was an increase in body height of 13 cm. or 3.6 cm./year. This was below normal for growth levels (16). In this same study Joslin noted a weight increase on the average of 2.2 Kg./year.

When insulin was discovered in 1922, and with the institution of insulin treatment, the diabetic child received a better prognosis, but it was still noted that there was a retardation in the physical development of these children. It has been shown by Wagner et al. (1942) that the development of hips, breasts, the appearance of pubic hair, occurred earlier in the short term diabetic than normal children used as controls(27).

Joslin et al. (1959) states that the age of menarche in diabetic girls was delayed to 13.96, but fertility rate remained high (17).

Joslin et al. (1925) reported that in an observation period of from 12-33 months of 69 diabetic children, an average gain in height of 2.3 inches was observed. This is compared to an average of 4.3 inches for the normal (16).

Ladd found growth retardation only when there was marked glucasuria of many months duration (18).

Spencer noted in his study of diabetic children observed for a period of 2.2 years that there was a growth retardation of 24% on the average (24).

Boyd and Nelson reported that the average rate of growth of 32 juvenile diabetics was slightly higher than the control group of non diabetic children (5).

Fischer (1929) in a study of 20 cases of juvenile diabetics found a 10% decrease below norms for body weight (9).

Robenowitch and Bozin in a study in 1929 found that in a study of 71 diabetic children there was a statistically significant decrease in rate of growth as compared to normal children.

It is important to note that the above investigations of growth in diabetic children were conducted in the early insulin era when a restricted diet, ie. low in carbohydrates and total caloric intake was being used as partial control of the diabetic. Such is not now the case, diets being much more liberal and

insulin dosages being much higher.

In the past years and especially since 1940, studies of growth of diabetic children indicate that growth usually proceeds quite normally but there is no general agreement as the following studies indicate.

Wagner and White (1942) in a very comprehensive account of growth disturbance in 1407 diabetic children report that 118 were retarded in growth for their age, according to the Englebach standard. The remaining 91.7% were reported to have developed normally (27).

In a study of diabetic children conducted by Beals (1948), she reported a significant difference in growth rates for diabetic children ages 5 years to 7 years, 2.25 inches compared to 2.63 inches for the normal. A lesser degree of difference was noted for ages 7 to 9 years.

Several authors are of the opinion that rate of growth is normal in insulin treated juvenile diabetics provided good control is maintained (5) (10) (15). No criteria for degree of control given.

Brown (1940) did not find any significant retardation of growth in diabetic children (7).

Bergqvist reports that Norwegian investigators, Engel and Andrup, found a definite retardation in growth curves for diabetic children. Engel's information was based on 53 cases all under 25 years of age, of which 10 were retarded below the

lower limits of normal for growth (3). Andrup, in his study (1935-1949) of 51 children with a history of disease prior to 13 years of age, found 13 to be retarded (3).

Bergqvist, in his Molino study of 56 diabetic children (29 boys and 27 girls), reports there is a tendency for girls to be more overweight than boys (3). The boys were more retarded in height than were girls, boys being retarded 4.1 cm. compared to 1.0 cm. for girls, the boys being observed for a period of 5.1 years, and the girls for 5.6 years average (3).

Bergqvist also states that in his study he could not substantiate the statement of White that diabetes in children has a tendency to appear after a period of more rapid growth (3) (29).

White states that diabetes has a definite effect upon puberty, peak age of onset is 10 years of age for females and 13 years for males, with an average of 11 years for both groups. This she attributes to the growth hormone (29).

In White's study, average height and weight at onset of diabetes was found to be 12 months in advance of chronological age, bone age was advanced 18 months and dental age was found to be 12 months advanced (29). These findings of White seem to support her statement of accelerated growth just preceding the diabetic period, which Bergqvist could not substantiate.

As stated earlier there is no agreement among the authors

cited that diabetes in children causes growth retardation.

Joslin, et al. (1959) report that in spite of a profound disturbance in the metabolism of glucose, linear growth appears to prodeed satisfactorily. They report that the median height finally attained by males in 1072 twenty-year survivals was 68 inches for males and 63 inches for females (17).

If juvenile diabetes is defined as the onset of diabetes prior to age 15, it is seen that the juvenile diabetic population constitutes approximately 5% of the total number of known diabetics (17). In the United States it is estimated there are 1,500,000 persons surviving their childhood form of the disease (17). It is further estimated that there is one child per 2,500 under 15 years of age who are diabetic. Joslin Clinic figures of 4,054 cases of juvenile diabetics record that 48.6% are boys (1,970) and 51.4% are girls (2,084). Girls seem to have an earlier onset, with a mean of 10 years, for boys it was 13 years of age (17).

White in 1959 reported of 94 diabetic children in which comparisons of height and weight were made with 74 now diabetic siblings. Between the ages of 5 and 16 it was found the averages per year were almost identical. Plotted on a Wertzil grid there was a very close approximation with each other in channels of growth and development (29).

White (1959) is of the opinion that growth hormone has a very definite influence on the juvenile diabetic with respect to growth, basing this on clinical and experimental observations (29).

GENERAL DISCUSSION OF PATHOGENESIS

Pathogenesis of growth retardation of diabetic children may be approached from several aspects. I have chosen to discuss only four areas which seem to me to be most important.

Nutrition

The low caloric intake of the diabetic child, a standard regimen in the pre-insulin era, leaves little doubt in one's mine that this was an important factor in the retardation of growth noted in these children.

Bergqvist in his study of 10 diabetic dwarfs, however, states that those dwarfs in his study were not undernourished but rather had a tendency to obesity (3).

Talbot et al., Lindeman and Kaufman in a study conducted in 1947 showed that even in significant undernutrition, growth can usually proceed at a cost of body fat (25) (19).

When diabetic children are given insulin therapy they begin to grow, less so in the early post-insulin era than at present (3). This may be explainable by the early post-insulin era practioners' tendency to cling to a low carbohydrate diet and low insulin dosage.

When caloric allowances for a given diabetic are calculated on the basis of age, height, sex, and physical activity, with an aim to provide sufficient calories for a normal growth, and with the judicious use of present day insulin, undernutrition

would seem to play but a minor role in retarded growth curves.

Deficient Control of Diabetes

Some authors, Ladd, Nelson and Jackson, feel that growth retardation is a result of poor control of the diabetic state, ie. severe hyperglycemia and prolonged glycosuria contribute to the retardation of growth curves (18) (5) (14).

Wagner in 1942 expressed a view in direct contrast to the above authors, stating that in his studies the control of retarded diabetic children was not less efficient than for the non retarded diabetic (27).

White, in the latest issue of Joslin's Treatment of Diabetes Melletus, states, "errors in the control of diabetes are often reflected in growth curves" (17).

Bergqvist in his study of 56 diabetic children and 10 diabetic dwarfs feels that poor control of the diabetes may result in growth retardation.

That groups of diabetic children vary in the frequency and degree of growth retardation is obvious from the foregoing reports, and probably the best explanation for such variation lies in the different methods of diabetic treatment.

Bergqvist poses a question. If lack of insulin per se and not necessarily via a disturbed carbohydrate metabolism gives rise to growth disturbance, how does this agree with clinical experience (3).

It would seem that a poorly controlled juvenile diabetic with marked glycosuria and hyperglycemia implies an insulin deficiency and would probably increase the tendency for retardation.

As mentioned earlier, a review of the development of diabetic treatment shows that in the pre-insulin era growth was inhibited in all except the very mild cases. To attribute this retardation soley to undernutrition as was popular, is not correct, except only in extreme undernutrition (19) (25) (16).

Nilman reports insulin is required for the anabolic effect of growth hormone on protein. This stemmed from studies of the relation of insulin and TSH on nitrogen retention using pancreatized and hypophysectomized pancreatized cats (21). Bergqvist reports some work by Young along the same line and found that when diabetes is produced by GH and even though the administration of GH is continued, there is no growth unless insulin is given (3).

Bergqvist's study of 56 juvenile diabetics shows that there is a slight retardation of growth curves after onset of diabetes and states that even under good control of the diabetic states, delayed growth seems to be a part of the total picture of the juvenile diabetic (3).

At present it would appear that the majority of authors feel that as exact a control as possible of the diabetes is necessary if one is to conteract the tendency for growth

retardation. It is questioned, however, that even under the strictest management is the body's lack of insulin fully compensated.

Hereditary Factors

That diabetes is a hereditary disease cannot be denied, and is probably transmitted by a Mendalian recessive trait (20). While this knowledge is of little benefit in the management of diabetes it does point up the necessity of keeping a close check on relatives of known diabetics.

Wagner found that from his studies of heights of parents of diabetic children with retarded growth that a familial predisposition for short or small stature cannot be the sole factor for the slow growth of the diabetic child (27). Bergqvist also gives some precedence to a "constitutional disposition of short stature" as a cause of under height, but is not willing to assign it full responsibility (3).

Sex Hormones (Gonadal insufficiency)

Albright, Talbot and Young in Bergqvist, Horstman and Hamburger are all in agreement that the testicular hormone has a marked effect on skeletal development (1) (3) (13) (11).

These authors attribute the effect of the testicular hormone to its stimulation of the proliferation of the epiphyseal cartilage and its accelerative action on bone growth and maturity, bringing about early closure of the epiphyseal lines and leading to cessation of growth.

Talbot states that hypofunction of the testes in adolescent boys does not result in obvious slow structural growth (25).

Hamilton reports that in a study of two castrated adolescent boys that the expected spurt of growth usually seen at adolescence did not take place (12).

Turner studied a series of young women who were described as hypogonadal and found them to be of short stature (26). However, he does not attribute the short stature to only hypogonadism. The relationship between ovarian hormones and growth stature has not definitely been proven as there are cases of hypogonadism without any somatic structural change (23).

The administration of estrogen to a true Turner's syndrome patient results in growth of the breasts, enlargement of the vagina, growth of the uterus, appearance of pubic hair and an increase in growth if the epiphyses are not closed. However, it seems that to attribute delayed growth to only gonadal insufficiency is incorrect (3).

Beal showed that retardation of growth in boys is more striking than in girls. This would be in agreement with the findings discussed above (2). Bergqvist finds this true in his study of 57 juvenile diabetics.

In summary, one may say that the greater tendency for retardation in boys as compared to girls may possibly be explained by gonadal dysfunction, ie. androgens are more important

for growth of boys than is estrogen for girls.

It is seen from the foregoing discussion that the aim in management of the diabetic child is to compensate as adequately as possible for the body's lack of insulin by insulin administration, if optimal growth is to ensue. One should strive to maintain blood sugar levels as near to normal values as possible and to avoid glycosuria without insulin reactions. Restriction of calories and carbohydrates in the diet must not be reduced to such a level as would circumvent as near optimal growth as possible.

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