Glucose Tolerance During the Menstrual Cycle

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SUMMARY

Oral glucose tolerance tests were carried out at weekly intervals in thirteen young women and six young men. There was a greater variation in response by the young women compared to the young men. This greater variation was due to altered responses during different phases of the menstrual cycle. It is suggested that the fluctuations in the oral glucose tolerance test during the menstrual cycle may be secondary to alterations in gastric activity. DIABETES *19*:450-52, June, 1970.

During the course of studies in this laboratory it was found that men and postmenopausal women showed an early increase in the concentration of glycerides in the fasting serum after a diet containing large quantities of sucrose, whereas premenopausal women showed no such response.[1,2] These findings, together with the variations in the fasting level of some serum lipids during the menstrual cycle[3,4] suggest that the response to a carbohydrate load may vary during the menstrual cycle. There are many reports of the variation, during the menstrual cycle, in blood sugar both fasting and in response to a glucose load,[5,6] and many of the findings are contradictory. We therefore decided to reinvestigate the serum glucose response during the menstrual cycle.

METHOD

Glucose was given by mouth at the level of 1 gm./kg. body weight, in 4 ml. water/kg. body weight, at four weekly intervals, to thirteen women aged twenty-one to thirty-two years (mean = twenty-four years) and to six men aged twenty to twenty-nine years (mean = twenty-five years). The subjects were all volunteers, the women being laboratory assistants or secretaries and the men being medical students or junior academic staff. No exclusion criteria except taking oral contraceptives were used. A sample of venous blood was taken after an overnight ten-hour fast, just before the glucose was taken. Venous blood was also taken at ¼, ½, 1, 1½ and 2 hrs. after ingesting the glucose. The onset of menstruation was considered as Day 1 of the cycle. Ovulation was not verified.

The glucose was estimated by an automated glucose oxidase method.[7]

RESULTS

The days of the menstrual cycle were arbitrarily divided into five groups, Days 1 to 6, 7 to 12, 13 to 18, 19 to 24, 25 to 29, and the mean and standard error of the glucose values in each of these intervals are seen in table 1. The results from the men are also shown in table 1.

To reduce the variation between subjects the mean of all the serum glucose values (mg./100 ml.) for each person when fasting was determined, and the difference from this mean of each fasting value in that person was expressed as a percentage, either positive or negative. An exactly similar procedure was carried out for each person on all values obtained at ¼, ½, 1, 1½ and 2 hrs. after the ingestion of glucose.

The percentage deviations of the glucose level at 0, ¼, ½, 1, 1½ and 2 hrs. for a person on one day were summed. Thus if the sum was negative it would indicate that for that day the glucose tolerance curve was better than the average for that person, and a sum that was positive would indicate that the tolerance was worse than average for that person. An example of the calculations is seen on the next page.

The variance of the sums of these percentage deviations in the glucose tolerance for all the days was calculated for both women and men.

Comparison of results from the men and women

The mean concentration of the fasting serum glucose for the women (fifty-two values) was 71.6 mg./100 ml. (S.E.M. ± 1.00) and for the men (twenty-four values) was 74.1 mg./100 ml. (S.E.M. ± 1.76). These two values are not significantly different.

When the variance of all the sums of the percentage deviation after glucose ingestion for each day for the women is compared with the similar value for the men,[8] there is a significant difference ($p = 0.02$ to 0.01). The variance is greater in the women (variance

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TABLE 1

The mean serum glucose values (and standard errors) after oral glucose in young women and young men. The values for the women are in groups relating to the first day of menstruation. The values for the men were obtained at weekly intervals for four weeks. n = number of tests.

Time (hours)	0	¼	½	1	1½	2	n
				Days 1 to 6			
x̄	76	97	96	76	71	79	7
± S.E.M.	2.5	5.7	8.6	8.8	6.0	4.5	
				Days 7 to 12			
x̄	71	97	86	70	71	69	12
± S.E.M.	3.1	3.5	5.3	3.9	4.4	5.1	
				Days 13 to 18			
x̄	71	103	107	83	75	73	10
± S.E.M.	1.8	2.6	6.8	5.8	5.1	3.9	
				Days 19 to 24			
x̄	72	100	104	75	74	67	12
± S.E.M.	1.9	3.9	4.9	4.1	4.6	4.6	
				Days 25 to 29			
x̄	72	100	90	74	72	70	11
± S.E.M.	1.8	4.4	5.7	4.1	5.3	3.4	
				Males			
x̄	74	98	114	101	84	76	24
± S.E.M.	1.8	5.3	4.5	5.9	4.8	3.2	

Subject A.E. Female 21 years old

Day of menstrual cycle	0	¼	½	1	1½	2	
	Serum glucose mg./100 ml.						
1	72	94	83	53	62	52	
7	60	90	62	50	75	48	
16	71	112	131	55	57	64	
28	66	90	58	55	65	57	
Mean	67	97	84	53	65	60	
	Per cent deviation from mean						Sum of per cent deviation from mean
1	+ 7.5	− 3.1	− 1.2	0	− 4.6	+20.0	+18.6
7	−10.4	− 7.2	−26.2	−5.7	+15.4	−20.0	−54.1
16	+ 6.0	+15.5	+56.0	+3.8	−12.3	+ 6.7	+75.6
28	− 1.4	− 7.2	−31.0	+3.8	0	− 5.0	−40.8

= 3,175) than in the men (variance = 1,480), thus suggesting that in the women's results there is at least one variable present which is not seen in the men's results.

Variations of the results during the menstrual cycle

When the menstrual cycle is arbitrarily divided into intervals of six days from the first day of menstruation it is found, using Student's *t* test, that the sum of the percentage deviations from the mean in the serum glucose is significantly raised ($p = 0.05$ to 0.025) in the period Days 13 to 18 inclusive (table 2). When this value for Days 13 to 18 is compared with that from the other intervals it is not significantly different except for the Day 7 to 12 value which is significantly less ($p = 0.01$ to 0.005) than the Day 13 to 18 value.

There is a significant increase ($p = 0.025$ to 0.01) in the one-half-hour serum glucose value ($\bar{x} = 107$ S.E.M. ± 6.8) at Days 13 to 18 when compared with the one-half-hour value at Days 7 to 12 ($\bar{x} = 86$ S.E.M. ± 5.3).

The highest single glucose level at one-quarter hour was found in the Day 13 to 18 interval in six out of the ten female subjects tested during this time, whereas one-half hour after ingestion of the glucose eight of the subjects showed their highest glucose level during the Day 13 to 18 period. At one hour only four of the subjects recorded their highest glucose concentration at this time during the Day 13 to 18 period.

DISCUSSION

It was stated earlier that the variance of the changes in the serum glucose level after ingestion of glucose was significantly greater in the women than in the men, thus suggesting that at least one additional variable was operating in the women. If this additional variable was the swing in hormonal level seen in women, then the variance of the various periods into

TABLE 2

The mean (and standard error) of the percentage deviation in serum glucose concentration after a glucose meal. n = number of tests.

Days from onset of menstruation	1-6	7-12	13-18	19-24	25-29	Males
Mean	—3.3	—29.3	+34.5	+1.5	—1.4	—0.3
± S.E.M.	26.22	15.60	16.41	16.35	13.20	8.98
n	7	12	10	12	11	24

which the menstrual cycle has been arbitrarily divided should not be significantly different from that in the men over-all. This is found to be so.

It has been shown that the rate of gastric emptying suddenly increases in the middle of the menstrual cycle and gradually and consistently decreases until the middle of the ensuing cycle, when it suddenly increases again.[9] If the values in this paper for percentage deviation in glucose tolerance are plotted against time, starting at Day 14 and ending at Day 13, then a highly significant slope becomes apparent (figure 1). Thus the alterations seen in the glucose tolerance during menstruation could be accounted for by the changes in the rate of gastric emptying seen during the menstrual cycle.

There are, for each individual, six values which contribute to the sum of the percentage deviation for each glucose tolerance test. If, therefore, this sum is divided by six, the mean percentage deviation in glucose level following oral glucose would be obtained. When the mean percentage deviation in glucose level is plotted against the day of the menstrual cycle, starting at Day 14 and ending at Day 13, the slope of the regression line thus obtained (b = —0.5 S.E.M. ± 0.16) is similar to the percentage change in volume of meal passing the pylorus after test meals during the menstrual cycle (b = —0.4 S.E.M. ± 0.11). This would tend to support the view that the alterations in the glucose tolerance curve during the menstrual cycle may be the result of the hormonal influences on gastric activity rather than on glucose metabolism. A recent paper[6] reported that glucose tolerance is greatest in the earliest phase of the menstrual cycle and the authors put forward the possibility that endogenous estrogen is in some way associated with the pattern of decline in glucose tolerance during the menstrual cycle. These findings are not in entire agreement with those reported here, and statistical analysis of the area under the glucose curves reported by these authors fails to reveal any significant difference and thus does not support the "pattern" of the glucose tolerance changes they saw.

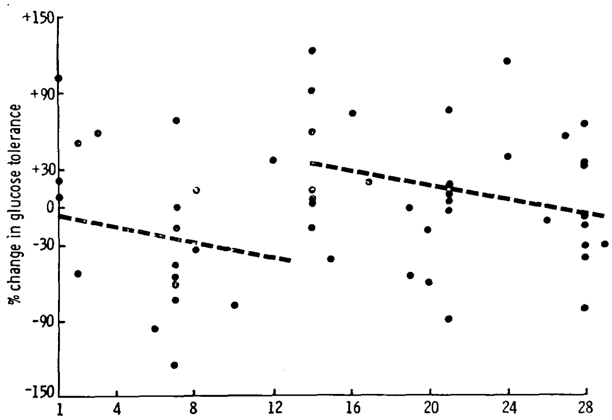

FIG. 1. The sum of the percentage deviations from the mean of all glucose values for each young woman plotted against the days of the menstrual cycle. The broken line is fitted to the data by the method of least squares.

Thus it seems that there is a variation in the oral glucose tolerance test which is associated with the menstrual cycle and this, it is suggested, may be secondary to the influence of hormones on the gastrointestinal tract.

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