Screening For Gestational Diabetes Mellitus: Comparison Of A Glucose Polymer And A Glucose Monomer Test Beverage

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Abstract: ***Background:*** **The current test for gestational diabetes mellitus (GDM) uses a glucose monomer test beverage, which frequently causes gastrointestinal symptoms, and venipuncture. We investigated a simplified test using a beverage of glucose polymer and a capillary whole blood glucose measurement.**

Methods: **In a randomized, double-blind clinical trial, women at 24 to 28 weeks' gestation received a 50-g glucose monomer (n = 41) or glucose polymer (n = 35) beverage. Venous and capillary blood samples were obtained 1 hour later. The women then completed standardized questionnaires about their symptoms.**

Results: **The glucose polymer beverage was associated with significantly fewer symptoms than was the glucose monomer drink: the mean was 1.1 symptoms per test with the glucose monomer drink and 0.4 symptoms per test with the glucose polymer drink ($P < 0.05$), 51 percent of the women developed symptoms after drinking the glucose monomer beverage, and 27 percent of the women developed symptoms after drinking the glucose polymer beverage ($P < 0.05$). Glucose type did not affect the 1-hour plasma glucose level, mean 5.94 mmol/L (107 mg/dL) for the glucose monomer and 5.76 mmol/L (103.8 mg/dL) for the glucose polymer ($P = 0.79$). For the capillary test, sensitivity was 0.75 and specificity was 0.82 in detecting a screening test positive by the venous plasma glucose criterion.**

Conclusion: **The results of this study indicate that a glucose polymer beverage is better tolerated than a glucose monomer beverage during GDM screening, but capillary glucose measurement might be of limited use in clinics where many personnel perform the capillary blood glucose testing. (J Am Board Fam Pract 1992; 5:241-7.)**

Gestational diabetes mellitus (GDM) complicates 2 to 3 percent of pregnancies in the United States.[1] Using factors in the health history, such as age older than 25 years, obesity, history of GDM, and adverse obstetric history, O'Sullivan, et al. found that these criteria detected fewer than 60 percent of women with gestational diabetes.[2] This low sensitivity prompted the Second International Workshop-Conference on Gestational Diabetes Mellitus to recommend universal prenatal testing of women for GDM.[1] The workshop-conference endorsed screening with a 1-hour, 50-g oral glucose challenge test at 24 to 28 weeks' gestation. If a woman's venous plasma glucose is equal to or greater than 7.8 mmol/L (140 mg/dL) 1 hour after glucose ingestion, the second step is an oral glucose tolerance test (OGTT) for diagnosis.[3] The study presented here was prompted by the desire to investigate modifications of the standard screening test in an effort to reduce the burden on staff and patients created by universal screening for GDM.

The standard test beverage used for the glucose challenge test, a mixture of glucose monomer, water, flavor, and carbonation, is often associated with nausea, vomiting, dizziness, abdominal bloating, and headache.[4,5] Many of these adverse effects are related to the high osmotic load of glucose, which causes delayed gastric emptying.[6] This problem has led to research into alternative beverages that are better tolerated.

Lind and Hytten[7] in 1969 demonstrated that blood glucose response curves were similar in

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pregnant women after a 50-g test beverage of glucose or maltose. Court, et al.[8] subsequently studied the use of a glucose polymer to test for GDM. A 50-g loading dose of the glucose polymer, under fasting conditions, produced peak and 1-hour plasma glucose levels not significantly different from those recorded under identical conditions using the glucose monomer. Court, et al. submitted questionnaires to a subset of 26 patients and found the glucose polymer to be significantly better tolerated. Court, et al. also compared 100-g loading doses of glucose polymer with 100-g loading doses of glucose monomer under nonfasting conditions for screening. The mean plasma glucose level 1 hour after the test was not significantly different for polymer and monomer beverages when analyzed by a two-tailed t-test.[9]

Reece, et al.,[4] in a study of 61 women, determined that glucose polymer and glucose monomer produced equivalent plasma glucose peaks after 50-g loads and concluded that glucose polymer could be used for the glucose challenge test. He also found that women suffered less nausea with glucose polymer, but an unspecified number of women did not complete the symptom questionnaire.

Both Reece, et al. and Court, et al. used a mixture of glucose polymers prepared by degradation of corn starch (Polycose™, Ross Laboratories, Columbus, OH), which is commercially available and widely used as a nutritional supplement. Polycose™ is a mixture of 3 percent glucose, 7 percent maltose, 5 percent maltotriose, and 85 percent polysaccharides (4 to 15 glucose units long). The inexpensive powder is virtually tasteless and has an osmotic load one fifth that of glucose.

In another effort to make screening simpler, researchers have investigated solid-phase reagent strips and reflectance photometry to measure capillary glucose. Landon, et al.[10] and Weiner, et al.[11] both reported a high degree of correlation between venous plasma glucose levels and capillary whole blood glucose levels in pregnant women undergoing a glucose challenge test. Yoo and Chao[12] confirmed these findings and found that capillary blood sampling was better tolerated by patients.

We investigated a simplified screening test for gestational diabetes using a glucose polymer beverage and capillary blood sampling in a primary care clinic setting. Symptoms associated with glucose polymer were compared with those associated with glucose monomer. We did not focus on the equivalence of glucose monomer and polymer for use in the glucose challenge test, as their equivalence for glucose tolerance testing has already been demonstrated.[4,5,8,9]

In addition, using a reflectance meter, we compared capillary blood sampling and glucose measurement with venous sampling and laboratory glucose measurement in screening for GDM. These modifications in the screening test were compared with the standard glucose challenge test in terms of reliability, patient tolerance, and patient preference.

Methods

The research protocol was implemented from January 1988 to May 1990 at the Ketchikan Native Health Clinic in Ketchikan, Alaska, and Mt. Edgecumbe Hospital, Sitka, Alaska. Earlier approval by the Ketchikan Native Health Board and Southeast Alaska Regional Health Corporation was obtained. Health centers in Ketchikan and Sitka deliver comprehensive, free health care to native Alaskans residing in southeastern Alaska.

Native Alaskan women at 24 to 28 weeks' gestation, without a history of diabetes, made up the study population. All eligible women were invited to participate and informed consent was obtained. Participating women were randomized into two groups and received either a 50-g glucose monomer beverage or glucose polymer beverage (Polycose™) in a double-blind design. Randomization was achieved by using consecutive numbers from a random number table.

Each study participant was given a test beverage regardless of time of last meal. One hour after ingesting the test beverage, venous and capillary blood samples were obtained. The capillary glucose was immediately measured using glucose oxidase solid-phase reagent strips (Chemstrip bG™, Boehringer Mannheim Corporation, Indianapolis, IN) and a reflectance photometer (Accu-Chek II Meter™, Boehringer Mannheim Corporation, Indianapolis, IN).

The reflectance meters were calibrated with each new container of reagent strips using the manufacturer's instructions and verified using a standard glucose test solution. Using a spring-

loaded microlancet, the capillary blood sampling was performed by various clinic personnel, including registered nurses and laboratory staff.

The same personnel performed the capillary plasma glucose measurement. The venous samples were drawn into tubes containing sodium fluoride and centrifuged, and the plasma glucose was measured by the hexokinase method. A glucose challenge test with a 1-hour plasma glucose level measuring 7.8 mmol/L (140 mg/dL) or greater was considered positive as recommended by the Second International Workshop-Conference on Gestational Diabetes Mellitus.[1]

After blood sampling, study participants completed a standardized questionnaire about symptoms associated with the glucose challenge test and preference for venous or capillary blood sampling.

All study participants were requested to undergo a 100-g, 3-hour oral glucose tolerance test within 3 days of their glucose challenge test. Study participants also received their obstetric care at the testing clinic. The results were evaluated by the criteria of O'Sullivan, et al. modified for venous plasma.[2,3]

Appropriate statistical tests, including analysis of variance, analysis of covariance, t-test, chi-square, linear regression, correlation, and logistic regression, were used. The Mann-Whitney method was used to determine the area under the receiver operator characteristic curve.[13] We attempted by deduction to identify confounding variables that could obscure the association between gastrointestinal symptoms and test beverages. We included parity in the analysis of covariance when comparing mean symptoms experienced with the test beverages. While there are no data on the association of gastrointestinal symptoms during the glucose challenge test and parity, the latter is strongly associated with nausea and vomiting during early pregnancy.[14] Parity was included in the model of the association between the presence of a symptom and the type of test beverage by use of logistic regression. The statistical analyses were performed using Solo version 3.1 (BMDP Corp.).

Results

Subjects

During the study period from January 1988 to May 1990, 76 women entered the study protocol. The age, gravida, parity, weight, family history of diabetes, and gestational week of women in the glucose monomer and polymer groups were similar. Ten women (13 percent) did not complete the symptom questionnaire, but their baseline characteristics did not differ significantly from those with complete data collection. Accordingly, the available data were used for further analysis.

Effect of Test Beverages on Plasma Glucose

Drinking the two test beverages, glucose monomer and glucose polymer, resulted in mean 1-hour plasma glucose levels that were not significantly different. For all 76 women who entered the study, the mean 1-hour venous plasma glucose measurement after the glucose monomer beverage was 5.94 mmol/L (107 mg/dL) (confidence interval 5.51 to 6.37 mmol/L, or 99.3 to 114.7 mg/dL) and after the glucose polymer beverage, it was 5.76 mmol/L (103.8 mg/dL) (confidence interval 5.07 to 6.45 mmol/L or 91.3 to 116.2 mg/dL) ($P = 0.79$).

The mean 1-hour plasma glucose levels for the women who completed the symptom questionnaire were also not significantly different. Parity, prepregnancy weight, or amount of weight gain during pregnancy did not significantly affect this agreement when included in the model analyzed by analysis of variance.

Symptoms Associated with the Glucose Challenge Test

Sixty-six women completed the symptom questionnaire following the glucose challenge test. Women screened with the glucose polymer beverage reported fewer symptoms than those study participants screened with the glucose monomer beverage. The proportion of women experiencing any symptoms was lower in the glucose polymer beverage group, 9 of 33, compared with the glucose monomer test beverage group, 17 of 33. The odds ratio for women developing any symptom after drinking a glucose polymer beverage compared with a glucose monomer beverage was 0.33 (confidence interval 0.11 to 0.95) by logistic regression with parity included in the model ($P < 0.05$). Of the eight symptoms on the questionnaire, five had odds ratios of less than 1, signifying fewer symptoms associated with the glucose polymer beverage

Table 1. Symptoms and Side Effects Associated with Glucose Monomer and Glucose Polymer Test Beverages during a Screening Test for Gestational Diabetes Mellitus in Women at 24 to 28 Weeks' Gestation (n = 66).

Symptom or Side Effect	Glucose Monomer (n = 33)	Glucose Polymer (n = 33)	Odds Ratio	Odds Ratio 95% Confidence Interval	*P* Value
Number of patients with any symptom	17	9	0.33	0.11, 0.95	0.03*
Felt sick	4	0	< 0.01	NA	NS*
Felt nauseated	10	4	0.22	0.05, 0.90	0.03*
Headache	5	1	< 0.01	NA	NS*
Felt dizzy	5	2	0.34	0.06, 1.95	NS*
Felt bloated	6	4	0.61	0.51, 2.41	NS*
Felt tired	3	4	1.00	0.03, 6.65	NS*
Vomited	0	0	1.00	NA	NS*
Felt abdominal discomfort	2	0	0.42	0.03, 5.43	NS*
Mean number of symptoms per test	1.1	0.4			0.03†

NA = confidence interval is not applicable as it is not interpretable.
NS = not significant.
*Logistic regression with test solution and parity as independent variables.
†Analysis of covariance with adjustment for parity.

(Table 1). Only the difference in frequency of nausea had statistical significance at the $P = 0.05$ level with an odds ratio 0.22 (confidence interval 0.05 to 0.90).

The mean symptom scores associated with the two test beverages (the sum of all symptoms divided by the number of subjects) were significantly different, with a mean symptom score of 1.1 for those in the glucose monomer group and 0.4 for those in the glucose polymer group (analysis of covariance, adjusted for parity, $P < 0.05$). The 95 percent confidence interval of the difference in mean symptoms was 0.1 to 1.2 symptoms per screening test.

Effect of Blood Sampling and Glucose Measuring Techniques on Blood Glucose Measurement

There was a high degree of correlation between capillary whole blood glucose measured with solid-state reagent strip and meter and venous plasma glucose measured by the hexokinase method ($r = 0.82$, confidence interval 0.72 to 0.89). The mean difference between venous plasma glucose and capillary whole blood glucose was −0.04 mmol/L (0.7 mg/dL) (confidence interval −0.20 to +0.28 mmol/L, or −3.6 to +5.0 mg/dL).

Regression analysis of the capillary whole blood glucose levels and the venous plasma glucose levels, using a least-squares method, generated the line of best fit for the data:

Capillary whole blood glucose = 1.2 + 0.79 (venous plasma glucose)

The data from the two test beverages were pooled to generate a single regression line, as the separate regression lines for the monomer and polymer test beverages test for coincidence ($F = 1.4$, $P > 0.10$). The capillary whole blood glucose 95 percent prediction interval for a venous plasma glucose of 7.8 mmol/L (140 mg/dL) was calculated to be 5.4 to 9.3 mmol/L (97.3 to 167.3 mg/dL).

No cases of GDM were found. Sixty-two women (82 percent) completed an oral glucose tolerance test, including all women with a glucose challenge test result of 7.8 mmol/L (140 mg/dL) or greater. The mean glucose challenge test result for women who did not complete an oral glucose tolerance test was 6.06 mmol/L (109.2 mg/dL). Four women had a positive glucose challenge test with venous plasma glucose > 7.8 mmol/L (140 mg/dL) on the screening test. By receiver operator characteristic curve analysis and identification of the point closest to a true-positive rate of 1 and a false-positive rate of 0, the optimal cutpoint for capillary whole blood glucose measurement to detect women with a positive glucose challenge test, by venous plasma criterion, was 6.94 mmol/L (125 mg/dL).[15] This cutpoint resulted in the capillary blood test having a sensitivity of 0.75 and specificity of 0.82. The area under this curve is 0.83 (a test with the area of 1 perfectly

distinguishes between normal and abnormal conditions, whereas a test with the area of 0.5 cannot distinguish between these two groups).[13]

Blood Sampling Preference

Women were polled, immediately after venipuncture and capillary sampling, as to their preference of technique for blood sampling. Twenty-three women preferred venipuncture, 26 women preferred capillary sampling, and the remainder listed no preference. The proportions preferring one of the two sampling techniques were not significantly different ($\chi^2 = 0.314$, 1 *df*, $P = 0.575$).

Discussion

This investigation focused on symptoms experienced by women in the second trimester of pregnancy while undergoing screening for GDM with a glucose challenge test using the traditional glucose monomer beverage or a glucose polymer beverage. The glucose polymer beverage was associated with significantly fewer symptomatic women, and those who received the glucose polymer noted significantly fewer symptoms per test after adjustment of their symptoms for parity.

Although our study has confirmed previous research on using a glucose polymer beverage, there are several limitations to this investigation. Despite collecting more data than previous studies, our sample size was small. Our inability to find significant differences in most of the symptoms women experienced during the glucose challenge test using the two beverages could be due to the small sample size. The confidence intervals of the odds ratios for the symptom data were quite wide, which is also a function of the small sample size.

The dichotomous symptom response data result from the design of our questionnaire. This limitation prevented us from detecting differences in severity of symptoms between the beverages, because a mild and a severe symptom were both recorded as the simple presence of a symptom. It is possible that when symptoms were present with the polymer beverage, they were not as intense as with the monomer beverage.

The patient questionnaire was subjective in nature although it was based on complaints associated with the glucose monomer beverage as reported in the literature and by women previously screened for GDM in our patient population. None of the questions focused on symptoms associated specifically with the polymer beverage, as no specific symptoms had been identified by the previous studies. Our questionnaire contained an open-ended request for unlisted symptoms in an attempt to identify other morbidity. The only additional complaint that we collected was that one study participant thought the polymer beverage was "not sweet enough."

The capillary method of blood glucose determination gave a mean glucose measurement not significantly different from the venous plasma-based technique. The correlation between the blood glucose testing techniques was high. We cannot determine the ability of the modified screening test, using the capillary blood technique, to detect women who eventually are shown to have GDM by an abnormal oral glucose tolerance test because no cases of GDM were uncovered.

The sensitivity of the capillary method to detect an abnormal screening test as defined by a venous plasma glucose of 7.8 mmol/L (140 mg/dL) was 0.75. This finding compares unfavorably to a sensitivity of 0.93 found by Landon, et al.[10] Our specificity, 0.82, was also lower than that found by Landon, et al. The lower sensitivity could be a function of different definitions of a positive glucose challenge test. Landon, et al. used a plasma glucose cutpoint of 7.5 mmol/L (135 mg/dL), while we used the cutpoint of 7.8 mmol/L (140 mg/dL), as recommended by the Second International Workshop-Conference on Gestational Diabetes. Our test protocols were also different; in the Landon, et al. study only 1 nurse performed the capillary glucose measurement, and the reflectance meter was calibrated before each test. Our study used various personnel in two clinics, and the equipment was calibrated less frequently. Landon, et al. paid greater attention to detail, which might increase the accuracy of the capillary glucose measurement method but would also make using in-office capillary glucose reflectance meters much more cumbersome.

If capillary blood tests were substituted for venous blood tests in screening for GDM, one positive glucose challenge test would have been missed, although no cases of GDM would have gone undiagnosed in this population. Of more concern is the low specificity of the capillary blood method, which would cause 13 women with

normal glucose challenge tests by venous plasma glucose criterion to undergo full oral glucose tolerance tests if capillary blood glucose measurement were used. Any savings in test cost and patient morbidity by substituting capillary sampling for venous sampling would be offset by the larger number of women who end up undergoing a 3-hour oral glucose tolerance test.

The lack of patient preference for capillary sampling was surprising as capillary sampling is widely used for blood sampling in children and for repeated sampling in adults. Despite the generally held perception that capillary sampling is less invasive, women in this study did not prefer this method. Because our women were polled immediately after experiencing both blood-drawing techniques, their responses probably reflected their actual preferences. Whether this ambivalence to blood sampling technique is generalizable or a characteristic of Alaskan women cannot be discerned.

Conclusions

The results of this study indicate that a glucose polymer beverage is better tolerated by pregnant women undergoing screening for GDM than is the widely used glucose monomer beverage. The proportion of women with any symptom after drinking a glucose polymer beverage was 9 of 33 compared with 17 of 33 for those drinking a glucose monomer beverage, a significant difference ($P < 0.05$). The mean number of symptoms per test was also significantly less in the glucose polymer group (0.4) compared with that of the glucose monomer group (1.1) ($P < 0.05$). The mean 1-hour venous plasma glucose reading of the glucose polymer beverage group was not significantly different from that of the glucose monomer beverage group.

Capillary plasma glucose samples had a high correlation with venous plasma glucose samples ($r = 0.82$); mean difference was 0.04 mmol/L (0.7 mg/dL) (confidence interval −0.20 to +0.24 mmol/L, or −3.6 to +4.3 mg/dL). The sensitivity and specificity of the capillary-based test, however, raises concern about its clinical usefulness in clinics where many personnel perform the capillary blood glucose testing.

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