



Short Communication

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Effect of acute hyperglycemia on clotting time and relative plasma viscosity (RPV) during menstruation

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ABSTRACT

Menstruating females seem to bleed more when they ingest sugar or sugar containing substances. This study was carried out to determine the effect of acute hyperglycemia on clotting time and relative plasma viscosity during menstruation. Forty menstruating females from the St. Philomena School of Midwifery, Benin, Nigeria volunteered for the study. Following ethical approval from St. Philomena Catholic Hospital, blood samples were collected from the ante cubital vein; pre-ingestion, one hour and two hours post ingestion of glucose concentrations (39 g/200ml, 78 g/200ml). Fasting blood samples and post glucose ingestion blood samples were analyzed for Sugar, Clotting time and Relative Plasma Viscosity (RPV) using Standard laboratory methods. Results were analyzed with paired t-test and values of $p < 0.05$ were considered statistically significant. The result showed a statistically significant increase ($p < 0.05$) in clotting time and a decrease in relative plasma viscosity ($p < 0.05$) one hour after the intake of both glucose concentrations. Two hours after glucose intake, there was a decrease in clotting time towards the baseline and an increase in RPV towards the baseline. This study thus suggests that acute hyperglycemia increases clotting time and reduced RPV in menstruating girls. This may be the reason for the perceived sense of increased menstrual flow.

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Keywords: Clotting time, Relative Plasma Viscosity (RPV), menstruation, blood sugar.

INTRODUCTION

Menstruation results from a complex interaction between the hypothalamus, the anterior pituitary gland, the ovaries and uterus (Guyton and Hall, 2006) and it typically indicates that fertilization did not occur. In the absence of pregnancy, the fall of plasma progesterone concentration due to corpus luteum involution triggers menstrual endometrium remodeling, leading to shedding of its functional layer associated with bleeding (Pauline et al., 2013). This desquamation is linked and controlled by cyclical fluctuations

in the levels of follicle stimulating hormone, luteinizing hormone, estrogen and progesterone. However, despite this intrinsic hormonal effect, extrinsic factors such as diet and life style can still influence menstrual flow and cycle. Studies have shown that non-modifiable host factors such as ethnicity and potentially modifiable risk factors such as smoking, physical activity and alcohol may affect menstrual cycle outcome (Liu et al., 2004). Dieting, a self-induced attempt to restrict food consumption can result to low serum leptin and in extreme cases of dieting

such as anorexia nervosa there can be disturbance of ovulatory function and abnormal menstrual cycle (Franca et al., 2000). Furthermore, stress and overwhelming fluctuation in weight and has been found to affect menstruation. During stress, the increased secretion of cortisol causes functional menstrual abnormalities (Loucks and Redman, 2004). Functional menstrual abnormalities such as delayed or reduced flow menstrual flow are traceable to the decreased release of estrogen and progesterone occasioned by the increased secretion of cortisol.

Clotting time which is the required for clot formation is one of the tests carried out during blood coagulation test, in addition to bleeding time and thrombin time. Coagulation involves both cellular (platelet) and protein (coagulation factor) component (Furie and Furie 2005) i.e it involves the intrinsic and extrinsic pathway with both occurring simultaneously. Tissue factor initiates the extrinsic pathway whereas the contact of factor XII (Hageman factor) and platelet with collagen in the vascular wall initiates the intrinsic pathway. Clot begins to form about 15-20 seconds later, if the trauma to the vascular wall is severe and 1-2 minutes if it is not severe (Guyton and Hall, 2006). As the bleeding time is correlated with the platelet levels, studies show that during menstrual phase, platelet count decreased and bleeding time increased, whereas around mid-cycle platelet count increased and bleeding time decreased (Rajnee et al., 2010). Earlier studies have shown that increase intake of glucose increases clotting time (Moreno et al., 2000). Plasma viscosity is essentially a measure of plasma protein changes, its level can change in parallel with fibrinogen, especially in acute phase response (e.g., in acute ischemic events), but can also be influenced by the level of triglycerides (Gabor et al., 2008). Relative plasma viscosity is the flow rate of plasma relative to the flow rate of distilled water (Reid and Ugwu, 1987). It has been shown that blood viscosity and plasma

viscosity decreases during menstruation and peak at about 7th and 21st day respectively, but fibrinogen which is the major determinant of plasma viscosity is found to be higher during menstruation (Dapper and Dida., 2002). Increase in blood glucose has been shown to increase relative plasma viscosity in diabetic patients (Olatunji et al., 2008) i.e. diabetes is a procoagulable state. This study is aimed at determining the effect of ingestion of varying concentrations glucose on clotting time and relative plasma viscosity during menstruation, in a view to assessing the impact of sugar on the intensity of bleeding during menstruation.

MATERIALS AND METHODS

Forty menstruating subjects between the ages of 18 and 25 from the St Philomena School of Mid-wifery in Benin City, Nigeria volunteered for the study. Demographic and menstrual cycle data were obtained by using a semi-structured questionnaire. The inclusion criteria were subjects aged 18 to 25, second day of menses, regular menstrual cycle while the exclusion criteria were history of anemia, use of contraceptive, history of diabetes and history of coagulation disorder.

By 9.00 am, the subjects arrived the laboratory and they were allowed to settle down. Few minutes after, 6mls of their fasting blood samples were collected from the ante cubital vein using a 21 G bore needle in a 10 ml syringe. 2ml of the collected blood sample was then injected into a fluoride oxalate bottle and the other 4mls into another anticoagulated bottle. Thereafter, twenty of them were given 39 g glucose/200mls of water and the other twenty subjects were given 78 g glucose/200mls of water. Blood samples were again collected from the ante cubital vein using a 21 G bore needle in a 10 ml syringe at 1 hour and 2 hours following the ingestion of glucose solution. Blood Sugar was analyzed using a colorimeter, Relative Plasma Viscosity (RPV) was assessed by a method described by Reids and Ugwu (1987) and clotting time was assessed using capillary tube method.

Statistical analysis

Data were presented as mean± standard deviation using the Microsoft excel 2010 analyzed using the student's paired t-test.

Ethics

Ethical clearance was obtained from the Ethics and Collaboration Committee of the St Philomena Catholic Hospital where the study was done. Informed consent was also obtained from the subjects.

RESULTS

The mean age, height and weight of the subjects studied were 21.51±3.97 years, 1.59±0.11 m and 59.33±3.33 kg respectively. While the age range for menarche and menstrual cycle length were 12-14 years and 28-30 years

respectively. 36 (90%) experienced increased use of sanitary pads following ingestion of sugar solutions, while 4 (10%) observed no change in the number of sanitary pads used. None of the subjects experienced an increase in the number of days of menstruation following ingestion of sugary solutions.

The mean values for blood sugar after the ingestion of 39 g glucose in 200 ml of water and 78 g glucose in 200 ml of water were compared to the base line values and the blood sugar was found to be higher (p<0.05) at the 1 hour post ingestion of glucose solution at both concentrations (Table 1). However, the difference in blood sugar at 2 hours post ingestion of both solutions of glucose when compared to baseline was not statistically significant (p>0.05).

Table 1: Blood sugar (BS) levels before and after ingestion of 39 g of glucose/200mls water and 78 g of glucose/200 mls water.

BS (mg/dl) before and after ingestion of 39 g of glucose/200 mls water	BS (mg/dl) before and after ingestion of 78 g of glucose/200 mls water	Time (Hr)
88.22±4.26	88.18±3.14	0
144.12±2.13*	161.54±3.33*	1
91.23±2.86	90.47±2.68	2

Superscripts (*) depict significant differences between 0hr or baseline and 1hr and 2hrs after ingestion of glucose solutions and analyzed by Paired t- test at P<0.05.

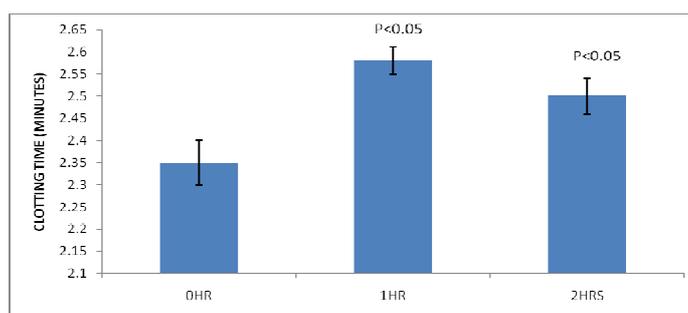


Figure 1: Clotting time at 1hr and 2hrs after the ingestion of 39 g of glucose/200 mls. The Clotting time value after one hour of the ingestion of 39 g glucose/200mls water during menstruation was significantly higher (p<0.05) than the baseline value. Similarly the two hour post ingestion of same concentration was significantly higher (p<0.05) than the baseline value.

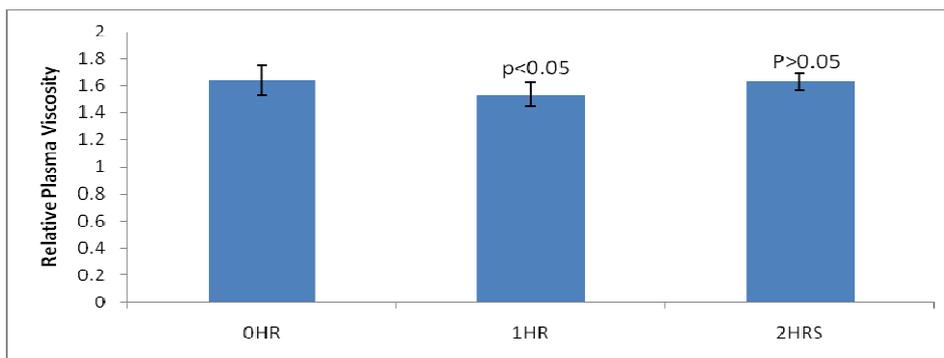


Figure 2: Relative plasma viscosity at 1hr and 2hrs after ingestion of 39 g of glucose/200 mls. The Relative Plasma Viscosity after 1 hr of ingestion of 39 g glucose/200mls water during menstruation was significantly higher ($p < 0.05$) than the baseline. However, the two hour post ingestion value was not statistically different ($p > 0.05$) from the baseline.

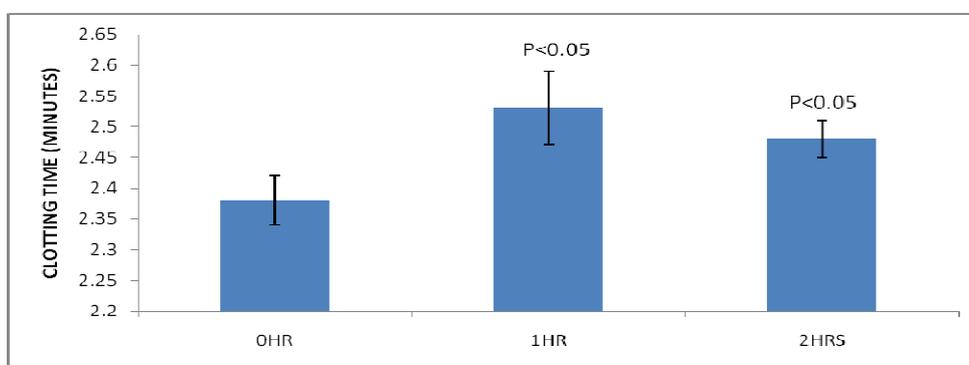


Figure 3: Clotting time at 1hr and 2hrs after ingestion of 78 g of glucose/200 mls H₂O. The clotting time followed the same pattern as that of ingestion 39 g glucose/200mls of water, despite the higher concentration of 78 g glucose/200mls of water.

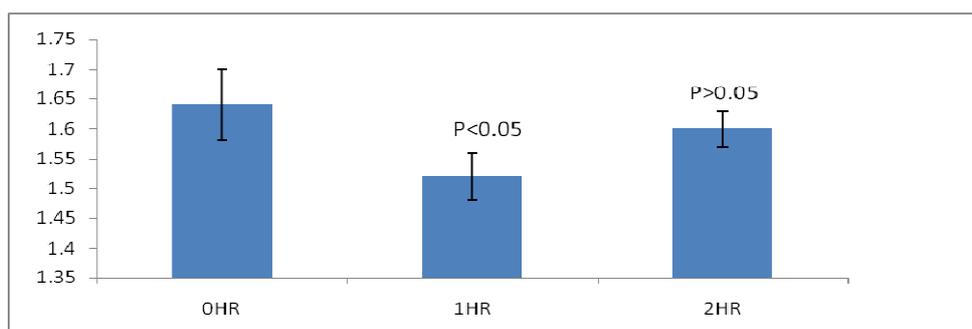


Figure 4: Relative Plasma Viscosity at 1hr and 2hrs after ingesting 78 g glucose/200 mls H₂O. The same pattern for RPV following ingestion of a lower concentration of glucose was observed i.e. the Relative Plasma Viscosity after 1 hr of ingestion of 78 g glucose/200mls water during menstruation was significantly higher ($p < 0.05$) than the baseline. However, the two hour post ingestion value was not statistically different ($p > 0.05$) from the baseline values.

DISCUSSION

The menstrual cycle is characteristically divided into four phases with each phase having associated hematologic changes (Omorogiuwa and Egbeluya, 2014). The phases are menstrual follicular, ovulation and luteal. The menstruation phase, which is the most obvious phase of the cycle, has been observed to be affected by sugar intake. However, most studies on the effect of sugar on coagulation factors have been on diabetic subjects. For instance, Sambola et al. (2003) reported that a circulating pool of tissue factor in blood associated with cells and microparticles is thrombogenic and is elevated in type 2 diabetes.

In menstruating girls there is evidence suggesting that there is reduction in platelet count which explains the increase in bleeding time and clotting time (Rajnee et al., 2010). Clotting time which is the time taken for blood to clot after an injury is a function of both platelets and plasma proteins. Plasma is a highly concentrated protein solution and its viscosity is determined basically by water content and macromolecular component of blood (Gabor et al., 2008). Among the plasma proteins, fibrinogen is the major determinant of plasma viscosity (Erdal et al., 2010). Results from this study showed a significant increase in clotting time during menstruation in accordance with a previous work done on this subject (Rajnee et al., 2010). The rise in clotting time in addition to the decrease in relative plasma viscosity from the ingestion of glucose may have increased the menstrual blood flow. Furthermore, acute hyperglycemia increases muscle blood flow and alters endothelial function in adolescents with type 1 diabetes (Amanda et al., 2012).

Menstrual endometrial breakdown induced by estradiol and progesterone withdrawal is regularly attributed to a sequence of vasospasm of the endometrial spiral arteries (Pauline et al., 2013), vasodilation in these vessels, increased blood flow and increased fibrinolytic activity. Although studies have shown that hyperglycemia in diabetics increases plasma

fibrinogen levels, relative plasma viscosity, blood viscosity and coagulability (Carr, 2001; Edem et al., 2010; Lemkes et al., 2010), the increase fibrinolytic activity of menstruation may have countered the hypercoagulable state of the induced acute hyperglycemia, consequently, reducing plasma viscosity and increasing clotting time (Figures 1, 2, 3, 4). The increase in clotting time during menstruation is as a result of the reduced platelet count (Rajnee et al., 2010). Nevertheless, the view on the effect of blood sugar on clotting time is divergent as Moreno et al. (2000) and Vijender (2006) revealed that sugar decreases the clotting time in the body.

Conclusion

From this study, the reduction in plasma viscosity increased clotting time and the increased endothelial blood flow following acute hyperglycemia may explain the increased menstrual flow experienced by the subjects. Since findings from this research suggest that glucose intake can lead to increase in clotting time and decrease in relative plasma viscosity with a perceived increase in menstrual blood flow, we recommend that females should reduce glucose intake during menstruation.

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