ORIGINAL RESEARCH PAPER

Volume-8 | Issue-5 | May-2019 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

EFFECT OF DIFFERENT PHASES OF MENSTRUAL CYCLE ON BLEEDING AND CLOTTING TIME IN 18-22 YEARS HEALTHY FEMALES.

Physiology

Bhavna Gupta Assistant Professor Department of Physiology, L.N. Medical College and J.k.Hospital, Bhopal, Madhya Pradesh, India.

Chhaya Batham* Assistant Professor Department of Physiology, Gandhi Medical College, Bhopal, Madhya Pradesh, India. *Corresponding Author

ABSTRACT

Background: Changes in the levels of female sex hormones during the menstrual cycle are known to affect the coagulation cascade by producing parallel changes in the prothrombotic tendency and the fibrinolytic activity of healthy women

Aim- The aim of present study is to access the changes in bleeding time (BT) and clotting time (CT) during different phases of menstruation which will suggest effect of female sex hormones over fibrinolytic activity of the blood. The correlation will help the surgeons for mastering elective surgeries.

Methodology: In present cross sectional descriptive study 140 healthy normal nursing students aging 18 to 22 years were considered. There BT and CT were accessed in four phases of menstrual cycle.

RESULTS- The mean BT and CT was least around the Ovulatory Phase or mid-cycle, raised during secreatory phase. Hence, we conclude optimal haemostatic testing and elective surgeries must be done in menstrual and early follicular phase.

KEYWORDS

Elective surgeries, Bleeding Time; Clotting Time; Menstrual Phase.

Introduction:

Menstruation is a physiological phenomenon which occurs in women during the reproductive epoch. . Bleeding Time and Clotting Time were accessed in four phases of menstrual cycle, i.e., menstrual phase, proliferative phase, ovulatory phase, and secreatory phase which are regulated by sex hormones, estrogen and progesterone from ovaries and also by gonadotropins: luteinizing and follicle stimulating hormones from anterior pituitary.[1]

During this menstrual cycle the hemostasis (i.e. the cessation of bleeding) is achieved through a delicate equilibrium between the coagulation and the fibrinolytic cascades. The formation of a stable fibrin clot is preceded and regulated by sequential activation of coagulation factors in events called the coagulation cascade.[2] Activation of blood coagulation is associated with accelerated clot formation, whereas activation of blood fibrinolysis enhances the breakdown of the blood clot. Intact hemostatic potential is essential for the control of menstrual bleeding.

Changes in the levels of female sex hormones during menstrual cycle are known to affect the coagulation cascade by producing parallel changes in the prothrombotic tendency and the fibrinolytic activity of healthy women. It appears that platelet function is increased during the luteal phase. There is also variation in the number of platelets and platelet retention during various phases of menstrual cycle.[3,4]

It is well known that onset of menstruation is preceded by sudden decrease in blood level of estrogen and progesterone about 2 days before and cessation of bleeding occurs with regaining of estrogen levels. Fibrinolysin (plasmin) present in the blood does not allow clotting and stasis of blood in uterus. Flow stops as a result of combined effect of vasoconstriction, myometrial contraction, and local aggregation of platelets.[5]

Hence, we had undertaken this study is to find out the effects of different phases of menstruation on Bleeding time and Clotting time. The findings of the present study not only will help the female candidates in the treatment of various systemic ailments and also in preparation of competitive sports and other such activities but also to surgeons to perform elective surgeries to reduce chances of excessive bleeding which will definitely reduce the possible hazards of blood transfusion.

Material and Method:

Present study is cross sectional descriptive study conducted in female nursing students from LN Nursing College, Bhopal.

Study protocol was submitted to Institutional ethical committee and ethical approval was sought. During data collecting study objectives and methods were explained to all participants using 'participant information sheet' that covered all the information of current study. Thereafter informed written consent was obtained from all the participants.

Inclusion criteria were normal healthy female aged 18 to 22 years with regular menstrual cycle (30 days ± 3 days) in previous six cycles and exclusion criteria were female with irregular menstrual cycles, subjects on oral contraceptives, anemic females, cases of any serious illness.

Sample size was calculated to be 140. Pretested semi structured questionnaire was used. Questions ware regarding history of irregular menstrual cycle, whether the subjects taking oral contraceptives, history of chronic respiratory illness. Other information obtained was present complaints, past history of any disease, surgery, menstrual history, history of drug use and family history.

The study was undertaken to assess bleeding time and clotting time in different phases of menstrual cycle. Menstrual cycle was charted for 6 months for confirming regularity. From the date of onset of menstrual cycle, probable date of ovulation was calculated, based upon which, different phases of menstrual cycle was determined. Subjects were asked to come on the 3rd, 13th and 21st days of menstrual cycle in the morning hours between 8.30 am to 9:00 am. If the calculated day fell on a holiday, then the subsequent cycle was taken.

Materials used for study includes sterile finger pricking, stopwatch, filter paper, capillary tubes. Data was entered and analysis using Microsoft office Excel 2007.

Bleeding Time was estimated by Duke Method whereas Clotting Time was estimated by Capillary tube method In Duke Method After taking all the aseptic precautions a skin puncture was made with the help of a sterile lancet and immediately a stop watch was started then the drop of blood was blotted on a circular filter paper every 30 secs taking care not to press on the bleeding spot. The drops became progressively smaller and stop in the end .The number of drops on the filter paper were counted and multiplied by 30 secs and thus the length of time required for bleeding to stop was recorded[17] (this method determines the functions of platelet and the integrity of the capillaries).

For clotting time the Capillary tube method was used in this method a sterile finger puncture was made using a lancet to the depth of 3mm, as soon as the blood was visible, stop watch was started. The first drop of blood was wiped off and the next drop of blood was collected in the capillary tube by introducing one end of the tube into the drop of blood while holding the other end at a lower level, the capillary tube was then held in the palms to maintain it at body temperature. After 2 minutes

the capillary tube was broken 1-2 cm from one end every 30 seconds and looked for the appearance of fibrin thread. When a thin string of fibrin was seen between the broken ends the stop watch was stopped and the time was noted.[18] Normal BT 2 to 5 min and Normal clotting time 3 to 5 min..

Result:
Following results were obtained

Table 1: Blood coagulation in different phases of menstrual cycle in seconds

Parameter	Proliferative Phase	Secretory Phase	Menstrual phase	F statistic	ANOVA p-value
Bleeding Time in seconds Mean (SD)	130.58 (39.06)	144.11 (28.64)	162.35 (25.45)	25.9630	<0.001
Clotting Time in seconds Mean (SD)	249.12 (40.45)	253.53 (53.34)	264.12 (39.61)	3.0060	0.0510

The results depicted in Table 1 were related to Clotting Time shows that longest clotting time measures in Menstrual phase as comparison to proliferative and secreatory phase. Shortest Clotting Time was found in proliferative phase. Also longest Bleeding Time in menstrual phase in comparison to proliferative and secreatory phase. Shortest Bleeding Time was found in proliferative phase. The p-value corresponding to the F-statistic of one-way ANOVA is less than 0.05 confirming the statistical significance.

Table 2: Post hoc test (Tukey HSD) results for Bleeding and Clotting time in different phases of menstrual cycle:

Different phases of menstrual cycle	Tukey HSD Q statistic		Tukey HSD p-value		Tukey HSD inference	
	Bleeding time	Clotting time	Bleeding time	Clotting time	Bleeding time	Clotting time
Proliferative vs Secretory	4.3247	0.9922	0.0068385	0.7428267	** p<0.01	Insignificant
Proliferative vs Menstrual	10.1537	3.3735	0.0010053	0.0463717	** p<0.01	* p<0.05
Secretory vs Menstrual	5.8290	2.3813	0.0010053	0.2132871	** p<0.01	Insignificant

The p-value corresponding to the F-statistic of one-way ANOVA is higher than 0.05, suggesting that the results are not significantly different for that level of significance. Those results also reflected on Tukey HSD (Honestly Significant Difference) test (post-hoc test) where all the difference was non significance in between groups except Proliferative vs Menstrual phase [Figure 3 and 4].

Figure 1: Bleeding Time in different phases of menstrual cycle in seconds

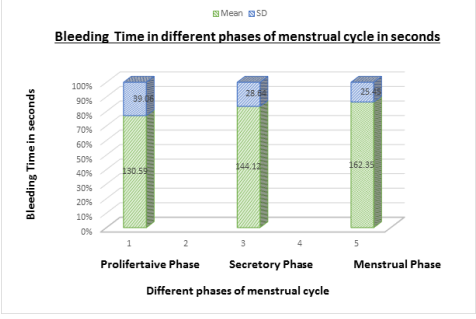


Figure 2: Frequency distribution of Bleeding Time in different phases of menstrual cycle

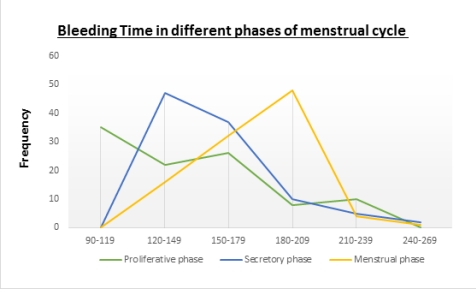


Figure 3: Clotting Time in different phases of menstrual cycle in seconds

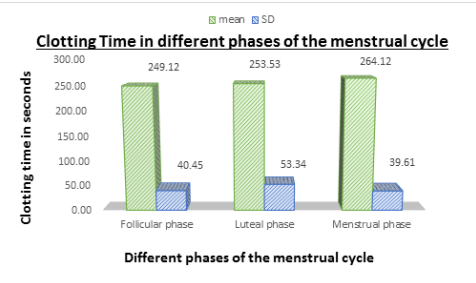
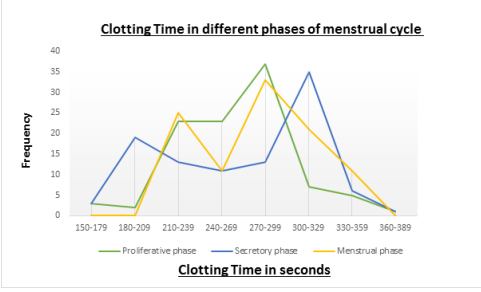


Figure 4: Frequency distribution of Clotting Time in different phases of menstrual cycle



Discussion:
Sex hormones play an important role in women's health. There are physiological variations in endogenous hormones during menstrual phase. Furthermore, use of exogenous hormones like oral contraceptives, hormone replacement therapy also plays a role in this variation.[6]

Physiological changes which occur during the course of menstrual cycle are mostly due to complex interactions essentially involving the hypothalamo-hypophyseal ovarian axis and the uterus. Almost all the changes are phase related and dependent on sensitive regulatory mechanisms. Variation in the functional parameters of many systems may be related to fluctuation in the hormone levels during the different phases of menstrual cycle.

In the present study, we found that mean Bleeding Time in proliferative phase was significantly ($P < 0.05$) less as compared to menstrual and secretory phases. It might be the combined effect of increased platelet count as well as aggregation, around the pre-ovulatory peak of estrogens during the proliferative phase.

In our study, we observed that mean Clotting Time in proliferative phase was 249.12 s, which was comparatively less than that observed at menstrual and secretory phases (i.e., 264.12 and 253.53 s, respectively), but the difference was not significant (p value > 0.05).[7,8] Some studies reported the lowest VonWillebrandFactor levels during menstruation or early follicular phase (cycle day 1–7). But few studies reported no cyclic variation of vWF. A cyclic variation of factor VIII is reported during menstrual cycle.[9,10]

Higher rate of coagulation and fibrinolysis was found among the endometrium of women with menorrhagia compared to women with normal blood losses. The hypothesis is supported by results of studies in which Tranexamic acid, an inhibitor of fibrinolysis, was administered to reduce the menstrual blood loss.[11]

Some studies reported the lowest fibrinogen levels during the follicular or mid-cycle phase. Few studies reported the lowest levels during the luteal phase and all other studies reported no cyclic variation. The

strong association between fibrinogen and the acute-phase reaction could be an explanation for this conflicting results.[12]

Yogita D Sulaxane et al conducted a study of cyclic fluctuation of Bleeding Time and Clotting Time in various phases of menstrual cycle. Their study showed that mean Bleeding Time at follicular phase was significantly ($p<0.05$) less as compared to that at menstrual and luteal phases. Their study concluded that primary and secondary haemostatic mechanism activities are at their high in the follicular phase than in the luteal and menstrual phases.[13]

In a study, conducted by Rajnee, Chawla VK, Choudhary R, Binawara BK and Choudhary S Bleeding Time and Clotting Time did not show any significant change during different phases of menstrual cycle. Bleeding Time and Clotting Time were least around mid-cycle, and thereafter they increased during secretory phase.[14]

Balasubramaniam[15] reported the shortening of Bleeding Time during the mid-cycle. The shortening of Bleeding Time around mid-cycle could be due to increase in platelet count. But the shortening of Clotting Time during the mid-cycle, though not significantly correlated with the platelet peak. The shortening of Clotting Time could be due to increased progestational compounds affecting clotting factors. Our observations are in contrary to some studies[16]in which no alteration was found in Bleeding Time and Clotting Time during different phases of menstrual cycle.

Conclusion:

As the Bleeding Time is correlated with the platelet levels, we found that during menstrual phase the Bleeding Time increased which probably may have been due to a decrease in platelet count, whereas around mid-cycle the Bleeding Time decreased. The shortening of Bleeding Time around mid-cycle could be due to probable increase in platelet count. The shortening of Clotting Time could probably be due to increase in progesterone compounds affecting clotting factors.

These cyclical changes in platelet aggregation and fibrinolytic activity suggest that there is prothrombotic tendency and low fibrinolytic activity during menstrual and secreatory phases which coincides with lower levels of oestrogen. Hence, we conclude optimal haemostatic testing and elective surgeries must be done in menstrual and early follicular phase.

REFERENCES

1. Guyton AC, Hall JE. Female Physiology before Pregnancy and Female Hormones. Pai RS, Prajna P, D'Souza UJA. Correlative study on blood pressure and lung function profiles during different phases of menstrual cycle among Indian population. Thai Journal of Physiological Sciences 2004; .
2. 2 Sanjeev Palta, Richa Saroa, and Anshu Palta Overview of the coagulation systemIndian J Anaesth. 2014 Sep-Oct; 58(5): 515–523. doi: 10.4103/0019-5049.144643: 10.4103/0019-5049.144643
3. Pai RS, Prajna P, D'Souza UJA. Correlative study on blood pressure and lung function profiles during different phases of menstrual cycle among Indian population. Thai Journal of Physiological Sciences 2004; 17(2):30-34.
4. Gulati N, Roy S, Malkani PK, Narula RK. Plasma protein bound iodine in normal menstrual cycle and in normal and abnormal pregnancy. J Indian Med Assoc1974;62(9):293-8.
5. C. Julian Dockeray, Brian L. Sheppard, Leisha Daly and John BonnarThe fibrinolytic enzyme system in normal menstruation and excessive uterine bleeding and the effect of tranexamic acid-*Eur. J. Obstet. Gynecol. Reprod. Biol., 24 (1987) 309-318
6. Greer JP, Foerster J, Lukens JN (Eds.). Wintrobe's Clinical Hematology,11th edn. Philadelphia, PA: Lippincott Williams & Wilkins, 2003.
7. Miller CH, Dilley AB, Drews C, Richardson L, Evatt B. Changes in von Willebrand factor and factor VIII levels during the menstrual cycle. ThrombHaemost. 2002;87:1082–3.
8. Feuring M, Christ M, Roell A, Schueller P, Losel R, Dempfle CE, et al. Alterations in platelet function during the ovarian cycle. Blood Coagul Fibrinolysis. 2002;13(5):443–7
9. Knol H, Kemperman RF, Kluin-Nelemans HC, Mulder AB, Meijer K. Hemostatic variables during normal menstrual cycle. ThrombHaemost. 2012;107:22–9.
10. Hahn L, Rybo G. Fibrinogen-fibrin degradation products in menstrual blood from women with normal and excessive menstrual losses. Acta Obstet Gynecol Scand. 1975;54(2): 119–27.
11. Gaur S, Datta S, Bhargava RP. Fibrinolytic activity, fibrinogen content, prothrombin time and clotting time during menstrual cycle. Ind J Physiol&Pharmacol 1982;26(2):152–6.
12. Sulaxane YD, Patel SG. Cyclic fluctuation of bleeding time and clotting time in various phases of menstrual cycle. Natl J Physiol Pharm Pharmacol 2015;5:328-332.
13. Rajnee, Chawla VK, Choudhary R, Binawara BK and Choudhary S. Haematological and electrocardiographic variations during menstrual cycle. J Physiol 2010; 6 (1): 18-25.
14. Balasubramaniam P, Parulkar VG, Bhatt JV. Some haematological observation during menstrual cycle. Indian J Med Sci 1980;3418:193–4.
15. Gaur S, Datta S, Bhargava RP. Fibrinolytic activity, fibrinogen content, prothrombin time and clotting time during menstrual cycle. Ind J Physiol & Pharmacol 1982;26(2):152–6.
16. Guyton and Hall. Text book for medical physiology, Philadelphia. Elsevier Saunders, Eleventh Edition, 2006; 467.
17. Bain B, Forster T. A sex difference in the bleeding time. Thromb Haemost. 1980; 18; 43(2): 131-2
18. Kadish A., Weisman H., Veltri E. 1990. Paradoxical effects of exercise on the QT interval in patients with polymorphic ventricular tachycardia receiving type Ia antiarrhythmic agents. Circulation; 81:14-19.