How to Cite:
Hoskatti, S., Hoskatti, D., & Pangi, M. (2022). Effect of handgrip exercise on QTc interval during different phases of menstrual cycle. *International Journal of Health Sciences*, *6*(S1), 5074–5083. https://doi.org/10.53730/ijhs.v6nS1.6027

Effect of handgrip exercise on QTc interval during different phases of menstrual cycle

Dr. Sachin Hoskatti
Associate Professor, Department of Medicine, Karnataka Institute of medical Sciences, Hubballi

Dr. Deepti Hoskatti
Tutor, Department of Physiology, Karnataka Institute of Medical Sciences, Hubballi

Dr Manish Pangi
Associate Professor, Department of Cardiac surgery, Sri Jayadeva Institute of Cardiovascular sciences & Research, Bangalore

***Abstract*---**Introduction: Menopause is a major change in a women's life, it refers to a permanent cessation of menstruation and fertility. The fast face of modern life has induced many problems like stress, anxiety, insomnia etc. associated with serious health problems. The most common disorders associated with menstruation among younger women are dysmenorrhea, pre-menstrual syndrome, menorrhagia, metrorrhagia. Aims and Objectives: To record the effect of handgrip exercise on QTc and RR interval in different phases of menstrual cycle and to compare with the baseline ecg values. Materials and Methods: The study was conducted on 40 medical (I MBBS) students from Mysore Medical College and Research Institute, Mysore. In this study a total of 40 female students aged between 17-19 years from 1st MBBS studying at Mysore Medical Collage and Research Institute, Mysore were selected as per the inclusion and exclusion criteria. Informed consent was obtained from each student. Data about the duration of previous two menstrual cycles and the days of menstrual bleeding were noted from the subjects statement. Subject monitored basal body temperature was used to identify phases of menstrual cycle. Ovulation was indicated by a sustained increase in the basal body temperature of at least 0.3°C after LH surge. Results: In our study Mean ± SD of RR intervals before handgrip exercise during menstrual, follicular and luteal phases are 809.5ms, 882.5ms and 872.25ms respectively. The values of mean RR intervals in the three phases after handgrip exercise were 955.5ms, 879.5ms and 870.5ms respectively. Mean ± SD of QT intervals before handgrip exercise during menstrual, follicular and luteal phases are 390.35ms, 374.5ms and 376.5ms

International Journal of Health Sciences ISSN 2550-6978 E-ISSN 2550-696X © 2022.
***Corresponding author**: Hoskatti, D.*
Manuscript submitted: 2 Dec 2021, Manuscript revised: 18 Dec 2021, Accepted for publication: 29 Dec 2021

respectively. The values of mean QT intervals in the three phases after handgrip exercise were 381ms, 380.28ms and 376.25ms respectively. Mean ± SD of QTc interval before handgrip exercise during menstrual, follicular and luteal phases are 435.77ms, 400.11ms and 405.04ms respectively. The values of mean QTc intervals in the three phases after handgrip exercise were 390.67ms, 407.96ms and 408.76ms respectively. Conclusion: Our study showed that there is cyclical variation of RR interval and QTc interval with menstrual cycle. The RR interval is decreased and QTc interval is prolonged during menstrual phase compared to follicular and luteal phases. The results of our study also showed that there is an increase in RR interval and a decrease in QTc interval after handgrip exercise during the menstrual phase as compared to follicular and luteal phases.

***Keywords*---**Handgrip exercise, QTc interval, Menstrual cycle.

Introduction

Menopause is a major change in a women's life, it refers to a permanent cessation of menstruation and fertility. The fast face of modern life has induced many problems like stress, anxiety, insomnia etc. associated with serious health problems. The most common disorders associated with menstruation among younger women are dysmenorrhea, pre-menstrual syndrome, menorrhagia, metrorrhagia, etc. [1] Apart from the menstrual problems women are susceptible to other disorders like cardio-vascular disorders, stroke, endocrinopathy, osteoporosis, anemia and other deficiency disorders. In the modern day, too much of stress results in greater predisposition to cardio-vascular disorders. Women are ten times more likely to die from cardio-vascular disorders than from others disease. One in eight women between the ages of 45 to 64 lives with cardio-vascular diseases. [2]

The hormones influence the cardiovascular system either directly by affecting repolarization or indirectly via the autonomic nervous system, the experimental studies provided evidence that the autonomic nervous system is modulated by estrogen. As the cardio-vascular system is constantly regulated by the sympathetic and para-sympathetic nervous system, any change in the autonomic activity enhances the risk of cardio-vascular disease and may trigger harmful events. [3] It has also been observed that the incidence of ventricular arrhythmias are more common in women and exhibit a cyclic variation in their occurrence with menstrual cycle suggesting a strong influence of sex hormones on the cardio-vascular system. [4]

Ovarian hormones may exert direct effects on the cardiovascular system. Treatment with estradiol can cause hyperpolarization in smooth muscles of dog's coronary arteries because of increased potassium conductance [5]. Estradiol may also have calcium antagonist properties. Women have slower cardiac repolarization than men, which manifests as longer heart rate corrected QTc [6]. This sex difference appears only after puberty [7]. Furthermore, women are more prone to develop ventricular arrhythmias after administration of drugs that

prolong cardiac repolarization (e.g. terfenedine and erythromycin) [8]. These findings suggest that the effect of drugs on ventricular repolarization can further be modulated by sex hormones possibly because they can alter potassium channel expression, ion currents, cardiac repolarization and QT responses to drugs [9].

Reflexes from contracting muscles affect the cardiovascular and respiratory system during exercise. It is well known that a sustained isometric contraction (SIC) induces an increase in heart rate, cardiac output, systolic blood pressure, diastolic blood pressure and pulmonary ventilation [10]. Heart rate and QT interval are the parameters which determine the rate corrected ventricular refractory period i.e. QTc. There is a cyclical variation in the ventricular refractory period during normal menstrual cycle [11].
Aims and Objectives: To record the effect of handgrip exercise on QTc and RR interval in different phases of menstrual cycle and to compare with the baseline ecg values.

Materials and Methods

This is a prospective and observational study conducted on 40 medical (I MBBS) students from Mysore Medical College and Research Institute, Mysore over a period of 1 year.

Inclusion criteria

- Young healthy female students from (I MBBS) Mysore medical college and Research Institute, Mysore.
- Age between 17-19 years.
- H/O regular menstrual cycles.

Exclusion criteria

- H/O menstrual abnormalities.
- H/O any Gynecological problems.
- H/O taking oral contraceptives.
- H/O medication during the study.
- H/O any cardiovascular disorders.
- H/O DM, HTN, Bronchial asthma and other Neuro endocrinal disorders or Syncopal attacks.

Instruments

The instruments used in this study are:

- Electro cardiograph (ECG)
  It is a single channel 12 lead electrocardiograph (Myocard-R) designed to produce accurate ECG.
- Handgrip dynamometers.
- Thermometer.

Method of collection of data

Data about the duration of previous two menstrual cycles and the days of menstrual bleeding were noted from the subjects statement. Subject monitored basal body temperature was used to identify phases of menstrual cycle. Ovulation was indicated by a sustained increase in the basal body temperature of at least 0.3°C after LH surge. The menstrual phase was based on subject's statement. On preliminary medical examinant, they were found to be physically fit, highly motivated and enthusiastic students. The physical anthropometric parameters were recorded.

All the study data were recorded more or less at the same of the day to avoid any possible diurnal variation effect (11am-1pm). The details of the procedure were explained and also demonstrated to the subjects in order to allay any apprehension.

The subjects were asked to lie down on a non-conductor comfortable bed for 10 mins before recording ECG. The baseline ECG was recorded and measurements of RR internal, QT internal were done using lead II. The QT internal was corrected for heart rate using Bazett's formula for rate corrected QT internal:

$$cQT = QT/\sqrt{R\text{-}R}$$

A handgrip sustained isometric contraction was performed in the supine position using a hand mechanical dynamometer. Initially each subject was familiarized with the experimental device and systematically trained. The subjects were asked to grip maximally with the dominant arm for a few seconds and this was repeated thrice. The highest value of the three contractions was taken as the maximum voluntary contraction (MVC). Handgrip was then maintained steadily at 30% MVC till fatigue. ECG record was taken within one minute of cessation of handgrip exercise.

Results

The percentage distribution of subjects with respect to SBP has been shown in table no.1.The percentage distribution of subjects in the three SBP groups i.e.110-114 mmHg, 115-119 mmHg and 120-124 mmHg are 20 %, 27.5% and 52.5% respectively.

Table 1
Showing the percentage distribution of subjects with respect to Systolic blood pressure

Systolic BP in mmHg	Number of subjects	Percent
110-114	8	20.0
115-119	11	27.5
120-124	21	52.5
Total	40	100.0

Table 2
Showing the percentage distribution of subjects with respect to Diastolic blood pressure

Diastolic BP in mmHg	Number of subjects	Percent
70-74	8	20.0
75-79	18	45.0
80-84	14	35.0
Total	40	100.0

The percentage distribution of subjects with respect to DBP has been shown in table no.2.The percentage distribution of subjects in the three DBP groups i.e. 70-74 mmHg, 75-79 mmHg and 80-84 mmHg are 20%, 45 % and 35 % respectively.

Table 3
Showing the percentage distribution of subjects with respect to Pulse Rate

Pulse rate in bpm	Number of subjects	Percent
71-75	9	22.5
76-80	22	55.0
81-85	7	17.5
85-90	2	5.0
Total	40	100.0

The percentage distribution of subjects with respect to PR has been shown in table no.3.The percentage distribution of subjects in the four PR groups i.e. 71-75bpm, 76-80bpm, 81-85 bpm and 85-90 bpm are 22.5%, 55 %, 17.5% and 5% respectively.

Table 4
Showing effect of Hand grip exercise on RR interval during the three phases of menstrual cycle

		Mean	No. of subjects	Std. Deviation	Std. Error Mean	T value	P value
Menstrual Phase	Pre HG Ex	809.50	40	89.670	14.178	-9.807	0.000*
	Post HG Ex	955.50	40	120.978	19.128		
Follicular Phase	Pre HG Ex	882.50	40	132.215	20.905	0.309	0.759^{-}
	Post HG Ex	879.50	40	117.276	18.543		
Luteal Phase	Pre HG Ex	872.25	40	131.549	20.800	0.362	0.719^{-}
	Post HG Ex	870.50	40	139.301	22.025		

*-Significant, $^{-}$-Not significant

Effect of handgrip exercise on RR interval during the three phases of menstrual cycle is shown in table no.4. Mean ± SD of RR intervals before handgrip exercise during menstrual, follicular and luteal phases are 809.5ms, 882.5ms and 872.25ms respectively. The values of mean RR intervals in the three phases after handgrip exercise were 955.5ms, 879.5ms and 870.5ms respectively. Paired T test was applied and it was found that there was significant rise in RR interval during the menstrual phase.

Table 5
Showing effect of Hand grip exercise on QT interval during the three phases of menstrual cycle

		Mean	No. of subjects	Std. Deviation	Std. Error Mean	T value	P value
Menstrual Phase	Pre HG Ex	390.35	40	28.794	4.553	1.471	0.149¯
	Post HG Ex	381.00	40	31.033	4.907		
Follicular Phase	Pre HG Ex	374.50	40	29.348	4.640	-0.907	0.370¯
	Post HG Ex	380.28	40	31.031	4.906		
Luteal Phase	Pre HG Ex	376.50	40	25.973	4.107	-1.638	0.109¯
	Post HG Ex	379.25	40	25.957	4.104		

*-Significant, ¯-Not significant

Effect of handgrip exercise on QT interval during the three phases of menstrual cycle is shown in table no.5. Mean ± SD of QT intervals before handgrip exercise during menstrual, follicular and luteal phases are 390.35ms, 374.5ms and 376.5ms respectively. The values of mean QT intervals in the three phases after handgrip exercise were 381ms, 380.28ms and 376.25ms respectively. Paired T test was applied and it was found that there was no significant change in QT interval during the three phases of menstrual cycle

Table 6
Showing effect of Hand grip exercise on QTc interval during the three phases of menstrual cycle

		Mean	No. of subjects	Std. Deviation	Std. Error Mean	T value	P value
Menstrual Phase	Pre HG Ex	435.77	40	39.258	6.207	6.588	0.000*
	Post HG Ex	390.67	40	22.963	3.631		
Follicular Phase	Pre HG Ex	400.11	40	19.720	3.118	-1.254	0.217¯

	Post HG Ex	407.96	40	41.286	6.528		
Luteal Phase	Pre HG Ex	405.04	40	23.529	3.720	-2.003	0.052^{-}
	Post HG Ex	408.76	40	25.275	3.996		

*-Significant, $^{-}$-Not significant

Effect of handgrip exercise on QTc interval during the three phases of menstrual cycle is shown in table no 6. Mean ± SD of QTc interval before handgrip exercise during menstrual, follicular and luteal phases are 435.77ms, 400.11ms and 405.04ms respectively. The values of mean QTc intervals in the three phases after handgrip exercise were 390.67ms, 407.96ms and 408.76ms respectively. Paired T test was applied and it was found that there was significant fall in QTc interval during the menstrual phase.

Table 7
Showing P value for RR, QT and QTc interval during the three phases of menstrual cycle

P value	Menstrual phase	Follicular phase	Luteal phase
RR interval	0.000*	0.759^{-}	0.719^{-}
QT interval	0.149^{-}	0.370^{-}	0.109^{-}
QTc interval	0.000*	0.217^{-}	0.052^{-}

*-Significant, $^{-}$-Not significant

Discussion

In our study the mean RR intervals before handgrip exercise during menstrual, follicular and luteal phases are 809.5ms, 882.5ms and 872.25ms respectively. This suggests that the resting RR interval is lower in menstrual phase than follicular and luteal phases. The results of our correlated with the study by Varshney VP and associates (2006)[12] in which lower RR interval was present during menstrual phase than the other two phases of menstrual cycle.

This could be explained because of lower value of estrogen during the menstrual phase. Estrogen is known for its vagotonic and sympatholytic action resulting in reduced heart rate in other words it increase RR interval. As estrogen is at its lowest value during menstrual phase the reverse is seen i.e. there is increase in heart rate in other words reduced RR interval during menstrual phase.

In our study the mean RR intervals before handgrip exercise during menstrual, follicular and luteal phases were 809.5ms, 882.5ms and 872.25ms respectively. The values of RR interval in the three phases after handgrip exercise were 955.5ms, 879.5ms and 870.5ms respectively. Paired T test was applied and it was found that there was significant rise in RR interval during the menstrual phase after handgrip exercise.

The results of our study are comparable with those of Varshney VP and associates (2006)[12]. They observed that women have lower basal RR interval during

menstrual phase as compared to follicular and luteal phases. They also observed that the RR interval increased significantly after handgrip exercise during menstrual phase.

In our study the mean QTc interval before handgrip exercise during menstrual, follicular and luteal phases were 435.77ms, 400.11ms and 405.04ms respectively. This suggests that the resting QTc is higher in menstrual phase than follicular and luteal phase. The results of our study are consistent with the study by Varshney and associates (2006) [12]. They observed that resting QTc was prolonged in menstrual phase than follicular and luteal phases. The present study differs from the study done by Rodriguez I and associates (2001)[13] wherein it was observed that there was no significant difference in the baseline QTc during the three phases of menstrual cycle.

In our study the mean QTc intervals before handgrip exercise during menstrual, follicular and luteal phases were 435.77 ms, 400.11 ms and 405.04 ms respectively. The values of mean QTc interval in the three phases after handgrip exercise were 390.67 ms, 407.96 ms and 408.76 ms respectively. Paired T test was applied and it was found that there was significant fall in QTc interval during the menstrual phase after handgrip exercise.

Our study results are comparable with those of Varshney VP and associates (2006) [12] wherein it was observed that QTc interval decreased significantly after handgrip exercise during menstrual phase.

In the menstrual cycle estrogen increases during follicular phase and progesterone level rises during luteal phase. Both these hormones are at nadir during menstrual phase. Thus there is a physiologically significant change in the circulating levels of estrogen and progesterone. These changes are suspected to prolong the baseline cardiac repolarization[14]. During menstrual phase low concentration of estrogen may increase sympathetic and depress para-sympathetic tone manifesting as a decreased RR interval. As the QTc is inversely related to RR interval there is an increase in QTc during menstrual phase under resting conditions[15]. Experimental data in animals show that oestradiol could decrease the function and expression of delayed rectifier outward potassium channels which regulate the repolarization phase of the cardiac action potential reflected by the QT interval.

Further, the QTc interval decreased significantly after handgrip exercise in menstrual phase whereas during the follicular and luteal phase there was a non significant rise in the QTc interval after handgrip exercise. This effect on QTc could be attributed to a lower serum K^+ level during the menstrual phase resulting in blunting of cardiovascular reactivity to stress.[16] In our study, the heart rate response to handgrip was blunted and following handgrip exercise, the heart rate instead of returning to baseline level fell below normal.

Gender difference in cardiac repolarization has been noted since the early part of this century. In a study by Burke (1997)[17] it was observed that the QTc interval was longer in women than men. In a study by Liu XL (2006)[18] observed that female rabbit ventricular myocytes have significantly lower I_{kr} and I_{kl} outward K^+

current densities compared to male rabbit ventricular myocytes, which contributes to the gender difference in QT interval.

Hence women are at a greater risk of developing drug induced adverse reactions(ADR) in the form of life threatening polymorphic ventricular arrhythmias due to administration of medications like class IA and III antiarrhythmic agents, antipsychotics, gastrokinetics, antihistamines, macrolide antibiotics, etc. that have the potential to block rapid delayed rectifier cardiac K^+ (I_{kr}) channels.

Conclusion

Our study showed that there is cyclical variation of RR interval and QTc interval with menstrual cycle. The RR interval is decreased and QTc interval is prolonged during menstrual phase compared to follicular and luteal phases. The results of our study also showed that there is an increase in RR interval and a decrease in QTc interval after handgrip exercise during the menstrual phase as compared to follicular and luteal phases. Thus we conclude that women are more susceptible to ventricular arrhythmias during menstrual phase, if exposed to drugs (like class IA and III antiarrhythmic agents, antipsychotics, gastroprokinetics, macrolide antibiotics, etc.) that have the potential to block rapid component of delayed rectifier cardiac K^+ (I_{kr}) channels which further prolong the refractory period. Our study showed that during the follicular and luteal phase the QTc is within normal limits thus pointing towards the cardio protective action of estrogen.

References

1. Ganong WF. Review of Medical Physiology, 22nd edi. Mc Grew-Hill Lange Medical Publications, Singapore. 2005; 440-443.
2. Guyton AC, Hall JE. Text Book of medical Physiology Eleventh edi, Elseveir, Saunders, Philadelphia, Pennsylvania. 2006; 1001-1026.
3. Drici, TR Barklow, V Hari Dasse, et al. Sex hormones prolong the QT interval and down regulate postassium channel expression in the rabbit heart Circulation, 1996;94(15):1471-4.
4. Altemus M, Roca C, Galliven E. Increased vasopressin and adrenocorticotropin responses to stress in the midluteal phase of the menstrual cycle. J Clin Endocrinol Metab 2001; 86:2525-2530.
5. Larsen JA, Kadish AH. Effect of gender on cardiac arrhythmias J Cardiovasc Electrophysiol, 1998; 9:655-64.
6. Abi Gerges N, Philp K, Pollard C, et al. Sex difference in ventricular repolarization: from cardiac electro physiology to Torsades de Pointes. Fundam clin Pharmacol, 2004; 18(2): 139-51.
7. Giuseppe ML, Rosano GM, Leonardo F, et al Cyclical variation in Supraventricular tachycardia in women. Lancet, 1996; 347:786-88.
8. Pham TV, Robinson RB, Danillo PJ, et al. Effect of gonadal steroids on gender related difference in transmural dispersion of L-type calcium currents. *Cardiovasc Res,2001;* 52: 752–762.
9. Korte T and Grohe C. Sex hormones and arrhythmia in myocardial ischemia. Britis J of Pharmacol. 2006; 146:227 – 228.
10. Carr BR. The normal menstrual cycle: the coordinated events of the hypothalamic –pituitary ovarian axis and the female reproductive tract. In

Carr BR, Blackwell RE, editors: Textbook of reproductive medicine, 2nd edi. Appleton and Lange, Norwalk, 1993;1448-56.
11. Yen SSC. The human menstrual cycle. In Yen SSL, Jaffe RB, Barbieri RL (Editors): Reproductive endocrinology 4th edi. Saunders, Philadelphia. 1999; 12-47.
12. Varshney VP, Bedi M, Bhandari B, et al. Effect of Handgrip exercise on QTc interval during different Phases of Menstrual cycle. Vascular disease Prevention, 2006:3:83-86.
13. Rodriguez I, Kilborn MJ, Liu YK, et al. Drug induced QT Prolongation in women during the menstrual cycle., JAMA 2001; 285:1322-1326.
14. Treloar AE, Bovnton RE, Borghild G.B, Et al. Variation of the human menstrual cycle through reproductive life. Int J Fertil, 1967; 12:77-126.
15. Collett ME, Wertemberger GE, Fiske VM. The effect of age upon the pattern of the menstrual cycle, Fertil steril, 1954; 5:437-448.
16. Noyes RW, Hertig AW, Rock J. Dating the endometrial biopsy Fertil Steril, 1950; 1:3-25.
17. Burke JM, Ehlert FA, Keuse JT, et al. Gender difference in the QT interval and the effect of the autonomic tone and menstrual cycle in healthy adults. Am J cardiol, 1997; 79:178-181.
18. Liu XK, Katchman A, Drici MD et al., Gender difference in the cycle – dependent QT and potassium currents in rabbit. J Pharmacol Exp Ther, 1998; 285 : 672 – 679.