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RESEARCH ARTICLE

Nerve conduction studies during various phases of menstrual cycle

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ABSTRACT

Background: Menstrual cycle is associated with hormonal fluctuations during various phases. Changes in estrogen levels are associated with swings in mood and cognitive functions. Against this background, this study was undertaken to observe differences in various parameters of nerve conduction during various phases of menstrual cycle. **Aims and Objectives:** Observe changes in sensory and motor nerve conduction during various phases of menstrual cycle. **Materials and Methods:** A cross-sectional study was carried out on 35 healthy female volunteers aged 18-35 years. Nerve conduction studies consisting of sensory and motor conduction velocity, distal latencies, compound muscle action potential amplitude, sensory nerve action potential amplitude, and the F wave latencies were carried out on ulnar, common peroneal, and the sural nerve during four phases of the menstrual cycle. **Statistical Methods:** Statistical analysis of the results was done using analysis of variance. **Results:** Nerve conduction parameters did not vary significantly with various phases of the menstrual cycle. **Conclusions:** Although synaptic conduction and release of neurotransmitters is modulated by estrogen and progesterone but these appear to have no significant role on the normal axonal conduction. Hence, no significant changes were observed in peripheral nerve conduction across various phases of the menstrual cycle.

KEY WORDS: Menstrual Cycle; Nerve Conduction; Changes; Variations

INTRODUCTION

Gonadal steroids have important modulatory effects on body fluid and electrolyte balance. Estradiol could modify the secretion of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) at the synapses, leading to delayed synaptic conduction time.[1] Progesterone influences nerve conduction and the susceptibility of peripheral nerves to the effects of local anesthetics.[2] In addition, progesterone has a thermogenic effect due to direct action on the hypothalamus.[3] Decrease in estrogen reduces neural conduction time and the availability of neurotransmitters.[4] Changes in the mood[5,6] or psychometric performance[7] have been reported during menstruation in normal women. Neurophysiologic studies have also demonstrated electroencephalogram (EEG) changes during the menstrual cycle.[7,8] However, there have been few reports of nerve conduction changes during the menstrual cycle.[9] Clinical observations suggest that ovarian hormonal changes modify auditory, olfactory and taste thresholds.[10,11] Some authors have found a significant increase in Brainstem auditory evoked potentials wave latencies associated with elevated levels of estrogen in the luteal phase (1), therefore, this study was undertaken to look for changes in nerve conduction parameters during various phases of the menstrual cycle.

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MATERIALS AND METHODS

Thirty-five healthy female volunteers with history of regular menstrual cycle in last 6 months (28±2 days), in the age group of 18-35 years and height 150-170 cm were recruited

for the study. Those with gynecological disorder or irregular menstrual cycles, diabetes mellitus, leprosy or other causes of peripheral neuropathy were excluded from the study. Female volunteers using hormonal contraceptives were also excluded. Written consent was obtained from all subjects. All cases were subjected to detailed history taking and thorough clinical examination along with recording of height and weight.

Various phases of menstrual cycle were differentiated using the calendar method. Day 1 of the cycle was considered when menstruation started. Ovulation was confirmed by serial sonography studies, performed on alternate days starting from the 10th day of the cycle. Nerve conduction velocity was measured using a portable, new generation, high precision 2-channel neuromyograph with inbuilt amplifier and computer, CANTATA TM model (manufactured by Dantec Elektronik, Denmark).

Nerve conduction studies in different phases were completed in one menstrual cycle. The same examiner performed nerve conduction measurements on all the subjects on 2nd day (menstrual phase), 7th day (follicular phase), 14th day (ovulation phase), and 21st day (luteal phase). Nerve conduction studies consisting of sensory and motor conduction velocity (NCV), distal latencies, compound muscle action potential (CMAP) amplitude, sensory nerve action potential (SNAP) amplitude, and the F wave latencies were carried out on ulnar, common peroneal, and the sural nerve.

The results were analyzed using the analysis of variance (ANOVA) test for repeated measurements and $P \leq 0.05$ was considered to be statistically significant.

RESULTS

A total of 35 subjects were studied. Age distribution of subjects is shown in (Table 1). Mean height of these subjects was 161.17±2.54 cm (Table 2). Duration of menstrual cycle was 27 to 28 days in 21 (60%) subjects and remaining 40% subjects had menstrual cycle ranging from 30 to 32 days.

Ulnar motor nerve conduction velocities and common peroneal nerve conduction velocities measured during various phases of the cycle have been depicted in (Tables 3 and 4), respectively. Highest value of ulnar motor nerve conduction velocity was observed on 14th day corresponding to the ovulatory phase but it was statistically not significant. Similar insignificant findings were also observed in NCV of common peroneal nerve (Tables 3 and 4).

Variation in distal latencies of both ulnar nerve and common peroneal nerve were insignificant (Tables 3 and 4).

Amplitude analysis of ulnar motor nerve revealed that the highest value was on 21st day (luteal phase), though the difference was insignificant. Minor variations were also recorded in the amplitude analysis of common peroneal nerve but statistically insignificant (Tables 3 and 4).

Table 1: Age of subjects

Age group in years	Number of subjects (%)
17-20	7 (20)
21-24	15 (43)
25-28	6 (17)
29-32	4 (11.5)
33-36	3 (8.5)
Total	35 (100)

Table 2: Height of subjects

Height (cm)	Number of subjects (%)
156-158	5 (14)
159-161	17 (49)
162-164	10 (28)
165-167	3 (9)
Total	35 (100)

F wave latency of ulnar motor nerve was highest during the menstrual phase but statistically insignificant (Table 3), whereas highest value in common peroneal nerve was recorded during ovulation phase, nevertheless, it was statistically insignificant (Table 4).

Sensory conduction velocity of ulnar nerve was highest on 21st day (luteal phase), but again statistically not significant when compared with values of other days. Similar findings were observed in sural nerve as well (Tables 5 and 6).

Ulnar nerve (sensory) amplitude (SNAP) across various phases was not statistically significant. However, sural nerve amplitude (SNAP) was the only parameter that showed significant variation with highest value being recorded during luteal phase (Tables 5 and 6).

DISCUSSION

Hormonal variations in different phases of menstrual cycle influence evoked potentials. Fluctuations in the level of estrogen and progesterone are responsible for the changes in the sensory processing and cortical excitability during menstrual cycle. Gonadal hormones can modulate neuronal excitability via effects on the ion channels.[1,12]

Several studies have shown that there is no significant variation in nerve conduction velocity from 19 to 40 years of age and nerve conduction velocities begin to decline only after the age of 40 years. Hence, we included women between 19 and 40 years in our study.[13]

Table 3: Ulnar (motor) nerve conduction studies

Parameters	Day of menstrual cycle					
	Day 2	Day 7	Day 14	Day 21	*F*	*P*
Mean motor NCV (m/s)	61.73 (5.60)	61.73 (6.22)	62.16 (5.96)	61.47 (5.18)	0.109	0.955
Mean distal latency (m/s)	2.51 (0.25)	2.42 (0.25)	2.46 (0.20)	2.45 (0.38)	0.725	0.810
Mean amplitude (mV)	4.96 (1.58)	5.22 (1.30)	5.18 (1.55)	5.33 (1.48)	0.518	0.671
Mean F wave Latency (ms)	24.66 (1.65)	24.58 (1.47)	24.17 (1.25)	24.44 (1.49)	1.009	0.392

Table 4: Common peroneal nerve conduction studies

Parameters	Day of menstrual cycle					
	Day 2	Day 7	Day 14	Day 21	*F*	*P*
Motor NCV (m/s)	59.43 (5.36)	57.71 (5.35)	58.35 (5.02)	58.13 (6.29)	0.77	0.51
Distal latency (ms)	4.29 (0.59)	4.15 (0.57)	4.16 (0.65)	4.12 (0.59)	0.77	0.51
Amplitude (mV)	3.99 (1.20)	3.99 (1.56)	4.19 (1.61)	4.51 (1.55)	2.27	0.085
F wave latency (ms)	41.53 (2.54)	41.33 (2.83)	41.69 (3.05)	40.65 (7.21)	0.49	0.69

Table 5: Ulnar (sensory) nerve conduction studies

Parameters	Day of menstrual cycle					
	Day 2	Day 7	Day 14	Day 21	*F*	*P*
NCV (m/s)	53.46 (6.84)	54.63 (6.31)	54.99 (5.82)	56.85 (5.77)	1.785	0.155
Amplitude (μV)	32.99 (9.27)	32.87 (8.52)	33.75 (5.95)	33.25 (7.76)	0.115	0.951

Table 6: Sural nerve conduction studies

Parameters	Day of menstrual cycle					
	Day 2	Day 7	Day 14	Day 21	*F*	*P*
NCV (m/s)	49.86 (6.72)	50.84 (5.97)	52.03 (5.77)	52.83 (5.87)	2.06	0.111
Amplitude (μV)	6.17 (3.08)	6.72 (2.73)	6.74 (2.65)	7.78 (2.51)	4.63	0.004

Height is an important confounding variable and an inverse relationship exists between the conduction velocity and height it reduces at the rate of 2-3 m/s for every 10 cm increase in height.[14] Subjects were evenly matched for height, 77% subjects had height in the range of 159-164 cm and height of all subjects ranged from 156-167 cm hence height is not a confounding variable in this study.

While comparing sensory conduction velocity for ulnar and the sural nerves, a steady subtle increase in the conduction velocity was observed starting from the menstrual phase to luteal phase, however, this was statistically not significant with $F = 2.03$ for sural and $F = 1.76$ for ulnar nerve.

Multiple comparisons of amplitude (SNAP) of the sural nerve at different times revealed that rise in SNAP amplitude was minimal up to the 14th day, and thereafter, a statistically significant increase was observed from 14th to 21st day, $F = 4.53$. Nevertheless, ulnar SNAP did not follow this pattern and had statistically insignificant finding with $F = 0.11$.

NCV and F wave latencies of common peroneal and ulnar nerves did not follow any pattern and the slight difference noted in different phases was statistically insignificant.

CMAP amplitude for both ulnar and common peroneal nerves showed peak values in mid luteal phase. Common peroneal nerve CMAP showed a gradual increase similar to SNAP for sural nerve. Ulnar nerve also followed almost the similar pattern but there was a slight aberration during midfollicular phase. However, these differences were statistically not supported by ANOVA analysis with $F = 2.22$ and $F = 0.51$ for common peroneal and ulnar nerve, respectively.

The gradual increase and peak values observed in conduction velocity and SNAP amplitude of sural nerve and CMAP amplitude of ulnar and common peroneal nerves can be attributed to increase in both estrogen and progesterone levels. Increase in levels of either hormone alone cannot explain these findings. If it was only estrogen then the peak should have been observed in mid cycle as against mid luteal phase seen in this study. Although a second peak of estrogen is seen in the mid luteal phase, it never reaches the levels

seen before ovulation. Progesterone alone cannot explain the above findings because its level start rising only after ovulation but it can definitely contribute to the increase in the conduction velocity due to its thermogenic effect.[3]

Progesterone produces neural effects independent of its hormonal activity.[15] *In vitro* studies have shown that progesterone and its metabolites rapidly inhibit nerve cell excitability by potentiating GABA mediated increase in chloride ion conductance.[16] Furthermore, data from animal experiments have shown that progesteronemetabolites enhance the action of GABA while estrogen has excitatory effects, possibly acting through theglutamate system.[12]

Characteristically, the basal body temperature (BBT) before ovulation is in the range of 36.1°C-36.3°C, and after ovulation, it is over 36.7°C in the luteal phase (1). Estrogen peaks in the late follicular phase associated with low body temperature while in the luteal phase both estrogen and progesterone levels were high associated with a rise in body temperature due to thermogenic effect of progesterone.[3] Conduction velocity increases at a rate of 1.2-2.4 m/s/°C rise in body temperature.[13] Increased temperature mainly alters the channel gating kinetics. Acceleration of sodium channel activation with warming increases conduction velocity, while the acceleration of sodium channel inactivation shortens the relative refractory period.[17] With decrease in temperature, there is consequent reduction in the sodium permeability of nerve axons during the excitation, resulting in a slower sodium influx and an increased latency (slow neural conduction). Decrease in temperature also increases the resistance to conduction of impulses which increase the latencies and decreases the conduction velocity.

BBT record was not feasible in this study as all the subjects were chosen from outpatient department. BBT needs to be measured immediately before getting up in the resting state and any activity or food intake is likely to change the BBT.

Nerve conduction parameters observed in this study were in the same range as those observed by Kimura, in normal adults.[13] A significant difference was observed only in amplitude of sural nerve 6.17±3.08 μV as against 18±10.5 μV recorded by Misra and Kalita, in normal adults without any evidence of neuropathy.[18] F wave latencies for ulnar and common peroneal nerves were also observed to be in the normal range.[19]

Our results are similar to the results obtained by Contreras et al., who had studied variations in EEG frequencies, reaction time, SSEPs, and nerve conduction velocities and they found no significant change in reaction time and nerve conduction velocity during the cycle.[20] In a similar study done by Juhi et al., who had studied nerve conduction velocity of median nerve during the different phases of menstrual cycle had found no significant change in nerve conduction velocity in relation to the phases of the cycle.[9]

Fluctuation in the levels of estrogen during the menstrual cycle could influence availability of GABA at the synapse and in turn influence conduction time.[1] Picton et al. had suggested that estrogen might influence synthesis and availability of acetylcholine at the synapses thus influencing nerve conduction.[4] These factors affect axonal conduction insignificantly in the peripheral nervous system, hence, no significant changes were observed in this study.

Effects of both estrogen and progesterone on renin-angiotensin-aldosterone system are divergent. Estrogen enhances angiotensin generation while progesterone is natriuretic by virtue of aldosterone antagonism.[21] There is increased urinary sodium excretion and this activates the renin-aldosterone system increasing sodium reabsorption thus restoring the serum sodium levels.[22,23] Bruce and Russel, on the other hand, had suggested that sex steroids lead to sodium and water retention in the luteal phase.[24] From these studies, it can be inferred that either serum sodium levels remain normal or they increase in the luteal phase.

CONCLUSION

It can be inferred from this study that the peripheral nerve conduction does not vary significantly during various phases of menstrual cycle. Some changes observed in nerve conduction were statistically insignificant except for the SNAP amplitude of the sural nerve. Although both hormones estrogen and progesterone have influence on some factors such as body temperature, electrolytes, and H+ ion concentration which have an effect on the nerve conduction, probably changes produced are short lasting, and therefore, have not significantly affected the nerve conduction parameters in this study. Further studies are required to establish the correlation if any between the hormonal peaks of estrogen and progesterone and peak nerve conduction velocity.

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