Cold Pressor Test, Moderate Anaemia in Second and Third Trimester of Pregnancy

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Abstract

Background: 2nd & 3rd trimester of pregnancy is associated with profound adaptive autonomic cardiovascular changes. Anaemia in pregnancy, which is a common problem in India is known to put pregnant female at higher cardiovascular risk.

Objective: The aim of this study is to measure & compare DBP response to CPT in both trimester in both control group & pregnancy with moderate anaemia (Case) for screening & diagnosis of autonomic imbalance.

Method: After measuring vitaldata, anthropometric data, DBP response to CPT were measured & compared among control & case group (13-39 weeks of gestation) in sitting position.

Result: A highly significant difference in Wt, SBP, DBP were observed in control group of 2nd trimester when compared with 3rd trimester. A highly significant difference was observed in Wt, DBP, DBP response to CPT of case group of 2nd trimester when compared with 3rd trimester; A highly significant difference was observed in Hb, SBP, DBP of case group of 3rd trimester when compared with control group during 3rd trimester of pregnancy;The chi-square test value shows that the observed DBP response to CPT in moderately anaemic pregnancy during 2nd & 3rd trimester is not due to chance.

Conclusion: This study has found CPT as simple, safe, cost effective, reliable test aiding to understand pathophysiology of anaemia during late gestation. It is also useful tool to predict & screen high risk pregnancy among anaemic pregnancies for early intervention.

Keywords: *Cold Pressor Test (CPT), Anaemia, Autonomic imbalance, Diastolic Blood Pressure (DBP).*

Introduction

A pre-eclampsia prevalence is of 7.5% of all pregnancies & it was found tobe slightly higher in primigravida[1] pregnancy with anemia[2,3], forms the base of doing our study in primigravida. Rang et al argued that since a higher sympathetic nervous activity has been observed in pre-eclampsia, changes in autonomic control preceding the onset of pre-eclampsia could provide early identification & it is essential for prophylactic interventions to reduce morbidity & mortality associated with this syndrome explains the aim of performing this study.[4,5] Different studies have been performed about the etiology of pre-eclampsia but there is no reliable & cost-effective screening test.[6,7] Although inflammation & extensive endothelial dysfunction of vessels are the main possible mechanisms of pre-eclampsia, but the pathogenesis of this syndrome has not been well understood.[6] Conducting this study in pregnant women with anaemia will aid to understand pathogenesis of this syndrome. The cold water causes stimulation of cold & pain receptors in the hand. The information is carried

to the brain through spinothalamic pathways. The reflex involves, rise in sympathetic outflow to the vasculature & heart resulting in rise in BP.[8] Results revealed that women when assessed at 12-20 weeks of gestation, who developed PIH subsequently, had heightened response to CPTin the form of more increase in both systolic & diastolic BP as compared to healthy pregnant women, who did not develop PIH.[9] Woisetschlerger[10] also had same observation & attributed this increase to increased vasoconstrictive response to physiological stimulus (cold).Studies show that significantly high incidences of development of PIH in late trimester in the healthy pregnant women who had shown higher cut off Values of BP response during CPT performed during early trimester of pregnancy, forms valuable objective for conducting our study to identify CPT as a routine screening test in pregnancy with moderate anaemia.[11]

Materials and Method: After obtaining approval from Institutional Ethical Comittee, CPT was performed in Applied Physiology laboratory from 9.00 a.m. to 11 a.m. at 24°C–26°C room temperature,of pregnant females (13–39 wksof gestation period) attending Antenatal Clinic of SMIMER Hospital, age 18-45 yr, with singleton pregnancy, who were ready to give written informed consent. In the control group, pregnant females with Hb level ≥11.0 g/dl & In a case group, pregnant females with moderate anaemia having Hb level between 7.0 g/dl to 9.9 g/dl, were assessed. For both group exclusion criteria were:

- H/o Multiple Pregnancy (e.g. Twins, triplets,etc.)
- H/o Significant illness of any system especially cardiovascular & Ventilatory System & other illness (e.g. malaria, asthma, tuberculosis)
- H/o Habit of smoking,drugs/alcohol intake or use of therapeutic drugs Esp. sympathomimetic drugs/ blockers.
- Females with pregnancy induced complication (e.g. Hypertension, Diabetes, Pre-eclampsia, Toxaemia of pregnancy).

Subjects were explained the procedure & were asked to avoid tea, coffee, food 2 hrs. prior to study. Anthropometric Data (height, weight) were measured on Standard Measuring Scale. Vital Data temperature, pulse rate, BP were assessed in supine position. **CPT (cold pressor test):** The test is performed in sitting position.[8] Digital BP instrument was calibrated with standard sphygmomanometer. First the baseline BP was measured using digital BP instrument & then the subject was instructed about the test. Cold water of 10°C was prepared & maintained at that temperature. The subject was asked to immerse the hand in water up to the wrist for 1 min. without touching the bottom of the cold water bath. After that the hand was removed from the water & it was covered with towel. The DBP was measured in contra lateral arm just before the hand was taken out of water. The DBP was taken again at 1.5 min & 4 min after the hand was withdrawn from the cold water. Highest DBP value was considered for calculation. Data were analysed using licensed SPSS 16.0 software. Statistical tests In dependant t–test, ANOVA (Mann–Whitney test), Chi–square test were used to analyse the obtained data. Results were considered significant at p value<0.05 & highly significant at p value<0.01.

Observation:

Table No. 1: Comparison of Mean of Parameters Between 2nd & 3rd Trimester (Control Group)

Parameter	Trimester	N	Mean	SD	p-value
Age (Years)	2nd	30	22.40	3.74	0.932
	3rd	46	22.32	3.30	
Hb (gm%)	2nd	30	11.36	0.50	0.085
	3rd	46	11.63	0.73	
Ht (cm)	2nd	30	150.90	5.23	0.417
	3rd	46	152.02	6.22	
Wt (kg)	2nd	30	48.56	12.82	0.0001*
	3rd	46	81.85	7.48	

Parameter	Trimester	N	Mean	SD	p-value
Pulse Rate (bpm)	2nd	30	90.40	10.80	0.464
	3rd	46	92.65	14.27	
SBP (mmHg)	2nd	30	104.33	9.26	0.006**
	3rd	46	96.10	14.15	
DBP (mmHg)	2nd	30	64.86	7.15	0.0001**
	3rd	46	109.58	12.85	
CPT (mmHg)	2nd	30	8.30	11.89	0.157
	3rd	46	5.27	6.46	

A highly significant difference in Wt, SBP, DBP were observed in Control Group of 2nd trimester when compared with 3rd trimester. No significant difference was observed in Age, Ht, Hb, Pulse rate, DBP response to CPT (Table No. 1).

Table No. 2: Comparison of Mean of Parameters between 2nd & 3rd Trimester (Case Group)

Parameter	Trimester	N	Mean	SD	p-value
Age (Years)	2nd	50	21.94	2.90	0.835
	3rd	52	21.82	2.88	
Hb (gm%)	2nd	50	9.06	0.79	0.949
	3rd	52	9.07	0.80	
Ht (cm)	2nd	50	150.18	5.06	0.102
	3rd	52	152.25	7.35	
Wt (kg)	2nd	50	47.10	5.49	0.0001**
	3rd	52	84.60	8.32	
Pulse Rate (bpm)	2nd	50	87.76	10.72	0.121
	3rd	52	91.07	10.67	
SBP (mmHg)	2nd	50	105.18	8.64	0.579
	3rd	52	103.94	13.27	
DBP (mmHg)	2nd	50	65.28	7.69	0.0001**
	3rd	52	91.09	13.89	
CPT (mmHg)	2nd	50	8.30	9.70	0.015*
	3rd	52	4.47	5.41	

A Highly Significant Difference was observed in Wt, DBP, DBP response to CPT of case group of 2nd trimester when compared with 3rd trimester; No significant difference was observed in Age, Hb, Ht, pulse rate, SBP (Table No. 2).

Table No. 3:Comparison of Mean of Parameters Between Case & Control Group (2nd Trimester)

	Group	N	Mean	SD	p-value
Age (Years)	Case	50	21.94	2.90	0.541
	Control	30	22.40	3.74	
Hb (gm%)	Case	50	9.06	0.79	0.000**
	Control	30	11.36	0.50	

	Group	N	Mean	SD	p-value
Ht (cm)	Case	50	150.18	5.06	0.545
	Control	30	150.90	5.23	
Wt (kg)	Case	50	47.10	5.49	0.480
	Control	30	48.56	12.82	
Pulse Rate (bpm)	Case	50	87.76	10.72	0.291
	Control	30	90.40	10.80	
SBP (mmHg)	Case	50	105.18	8.64	0.681
	Control	30	104.33	9.26	
DBP (mmHg)	Case	50	65.28	7.69	0.812
	Control	30	64.86	7.15	
CPT (mmHg)	Case	50	8.30	9.70	1.000
	Control	30	8.30	11.89	

Except Hb value, No Significant Difference in Age, Wt, Ht, Supine Pulse Rate, SBP, DBP, DBP response to CPT as observed in Case Group of 2nd trimester when compared with Control Group of 2nd trimester (Table No. 3).

Table No. 4: Comparison of Mean of Parameters between Case & Control Group (3rd Trimester)

	Group	N	Mean	SD	p-value
Age (Years)	Case	52	21.82	2.88	0.427
	Control	46	22.32	3.30	
Hb (gm%)	Case	52	9.07	0.80	0.000**
	Control	46	11.63	0.73	
Ht (cm)	Case	52	152.25	7.35	0.870
	Control	46	152.02	6.22	
Wt (kg)	Case	52	84.60	8.32	0.090
	Control	46	81.85	7.48	
Pulse Rate (bpm)	Case	52	91.07	10.67	0.535
	Control	46	92.65	14.27	
SBP (mmHg)	Case	52	103.94	13.27	0.006**
	Control	46	96.10	14.15	
DBP (mmHg)	Case	52	91.09	13.89	0.000**
	Control	46	109.58	12.85	
CPT (mmHg)	Case	52	4.47	5.41	0.051
	Control	46	5.27	6.46	

A Highly Significant Difference was observed in Hb, SBP, DBP of Case Group of 3rd trimester when compared with Control Group during 3rd trimester; But No Significant Difference was observed in Age, Ht, Wt, Pulse rate, DBP response to CPT (Table No. 4).

Table No. 5:Association of Value of DBP During CPT in Moderately Anaemic Pregnancy & in Healthy Pregnancy

AFT	Value	2nd Trimester			3rd Trimester		
		Control (n=30)	Case (n=50)	p-value	Control (n=46)	Case (n=52)	p-value
CPT (mmHg)	≥ 10†	13	20	0.769	21	21	0.598
	<10††	17	30		25	31	

† is considered as Normal response to Test., †† is considered as Abnormal response to Test.

The Chi-square Test value shows that the observed DBP response to CPT in moderately anaemic pregnancy during 2nd & 3rd trimester is not due to Chance (Table No. 5).

Discussion

CDKUOetal (2000) has described Biphasic Changes in Autonomic cardiovascular Control during Pregnancy which include higher Vagal & lower Sympathetic Modulation in the 1st trimester in Supineposition, because of increased Blood Volume, which is lasting upto mid-pregnancy. As gestational age increases further, Aortocaval compression caused by the Enlarging Gravid Uterus further compromises VenousReturn & CO,leading to a shift in Autonomic Nervous Activity towards an evenHigher Sympathetic & Lower Vagal Modulation in the 3rd trimester of Pregnancy.[12] which is observed during our study irrespective of level of Hbin Blood. There are reports of an increase in Resting Peripheral sympathetic Activity during 3rd trimester as measured by Peroneal Nerve Microneurography in patients withPIH as compared to Healthy Pregnant & Non-pregnant Females, Which returned to normal level in post-partum period.[13] It is generally accepted that the pre-eclampsia is characterised by the low Circulationg Volume & high Vascular Resistance[14,15] & also a higher CO was observed in early Pregnancy, who developed pre-Eclampsia later in pregnancy compared to healthy Pregnant Women.[16,17] this supports the high SBP value observed in our study group 2nd trimester of pregnancy with Moderateanaemia. There is increased refractoriness to Circulating Angiotensin II during normal Pregnancy, But women who destined to develop PIH or Pre-eclampsia have increased sensitivity to Angiotensin II, as a result of an Alteration in vessel wall Refractoriness rather than the Consequence of Changes in blood Volumeor Circulating renin-angiotensin Levels. Majortiy of study authors observed no Difference in Heart Rate between healthy Pregnant Woman & Pre-eclamptic Woman.[4] this explains unreliability of Heart Rate as a sole parameter to rule out High risk Case. Studies have shown that Neurovascular Transduction is generally Reduced in Normotensive Pregnancy, thereby dissociating Sympathetic Nerve activity from Vascular Resistance & arterial Pressure during CPT.[18] This explains the Variability in Observations of our Study. BP is maintained by CO & TPR;these two show Significant inverse Relationship that is, Higher the CO the lower is the Vascular Resistance. Sympathetic Nerves play a major role in regulating BP by Controlling the Resistance of the arterioles & the capacity of the Veins. During Cardiac function at Rest, they play only a minor Role in controlling the Strength & the Rate of the Heart Beat. During Physiological Stress however, increased Sympathetic Activity combined with Decreased Parasympathetic Activity increases the Rate & force of Contraction of the heart leading to an increase in CO.[19] MELANIE J BLAKE, Allison Martin et al (2000) has found that there occurs Significant change in supine SBP & DBP during different trimester in Normotensive Pregnancies[20], which is consistent with finding of our study. **Total Peripheral Resistance** (TPR) falls Significantly by at least 6 weeks of gestational age & reaches a Nadir of 40% below Non-pregnant Values by mid-gestation. Fall in TPR also makes CO to fall. The CO depends on patient position & is greatest when measured in Lateral Recumbent position. This is most notable during last Trimester. When, with the woman in supine Position, the gravid uterus & foetus impede venous Return (VR)to the heart. There is decrease inCO by 0.6 L/min in supine position. There is selective regional distribution of this Physiologic increase inCO. Uterine blood flow increases 10 fold to between 500 to 800 ml/min. Renal Blood Flow increases significantly by 50% during Pregnancy.[21,22] **BP** decreases in Pregnancy beginning as early as 7th week. This early drop probably represents incomplete Compensation of the fall inTPR by the increase in CO. When measured

in Sittingor Standing positions, SBP remains relatively stable throughout Pregnancy, whereas DBP decreases by a maximum of 10 mm Hg at 28 wks of gestation & then increases towards non-pregnant levels by term. In left Lateral position both decreases below Non-pregnant values at 24-32 wks of gestation[23,24]; which is not included in our study. The rise in Systemic Resistance & fall in CO without change in Arterial Pressure observed after assumption of the Upright posture in adult imply Peripheral Vasoconstriction & indicate that the circulatory changes of chronic Anaemia are labile rather than fixed.[25] explains the need to select stress test like CPT for our study group. The reduced BP response reported could be due to antagonistic effect of the products of the utero Placental unit, such as progesterone or a diminished Contractile Response of the blood vessels to Adrenaline[26] probably explains the low DBP response than the cutoff value while performing CPTin both the groups. No Significant difference in pulse rate observed in our study. Data suggested that Tachycardia & Increased flow Velocity are not physiologically adapted to prolonged strain but rather are mechanisms to meet acute bodily stresses such as fever,exercise, hyper metabolism & acute anaemia.[25] William B Porter et al[25] has described four mechanisms operating in anaemic patients which may increase the supply of oxygen to tissues when the oxygen carrying capacity of the blood is reduced;under conditions of rest, a rapid velocity flow & tachycardia with an increase in minute volume of CO is the first response to anaemia. As compensation develops, tachycardia & increased velocity flow are largely replaced by selective Shunting of blood & the removal of an increasing percentage of Oxygen in the tissue capillaries from each gram of circulating Hb. A reduction in TPR reduces cardiac work, thus tend to balance the effect of the elevation in CO. In patients with highest CO, tachycardia was not a prominent feature. Even breathing 100% oxygen show no change in elevated CO in anaemia.[25, 27] this supports our study result;the high SBP & low DBP observed during 3rd trimester of pregnancy with moderate anaemia. Martin et al[25] revealed that the severity ofChronic anaemia didnot correlate well with the level ofCO.They also revealed that the mean Venous Pressure was within normal limits for the anaemic Group & generally was unchanged after the therapy of Anaemia. The decreased Arterial Pressurein Anaemia might be a reflection of a number of events including generalised Vasodilatation & a reduced Bloodvolume. Maintenance of a normal Venous Pressure may well represent an effort to overcome these latter changes by Vasoconstriction & increasing the return of blood to the heart. The acute, immediate reversal of the high Output state of Anaemia by orthostatic Stress or by vasoconstrictor Drug indicates that the increased Blood flow is primarily mediated by lowered Peripheral Resistance due to vasodilatation rather than to low Blood Viscosity.[28,29]It has been postulated that the Hyperkinetic Response to anaemia in patients at rest occurs only when the Concentration of Hb falls beneath 7 gm/dl[30] explains the role of CPT to find out underlying Subclinical pathogenesis. Martin Duke et.al.[25] had revealed that in many patients, the hemodynamic values that appeared within normal limits in the Anaemic state were actually Altered when compared to that particular individuals normal state after therapy;explains the objective of performing this study.

Conclusion

This study has found CPT as simple, safe, cost effective, reliable test aiding to understand Pathophysiology of Anaemiaduring Late Gestation. It is also useful tool to Predict & Screen high risk Pregnancy among Anaemics for early Intervention. Many such studies & further evaluation are needed to support our observation forms the limitation of our study.

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Conflict of Interest: Nil

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