



# Transcranial Doppler study of cerebral hemodynamic response to graded Valsalva maneuvers in young healthy females.

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## ABSTRACT

**Background-** The Valsalva maneuver is commonly performed during everyday activities such as lifting, defecation and coughing, and is characterized by changes in intrathoracic pressure that have a pronounced effect on venous return, cardiac output and blood pressures.

**Aims and objective-** To study the cerebral hemodynamic response to graded Valsalva maneuvers (VM) in young healthy females.

**Material and methods:** Thirty young female participants were recruited for the study. A common familiarization session was arranged for the participants. During the familiarization session the participants were familiarized with all experimental procedures and equipment, including practicing Valsalva maneuvers

**Results:** Comparison between mean arterial blood pressure (MAP) and Middle cerebral artery MCAV<sub>mean</sub> of baseline, 90%, 30% and after VM were done and in all variables, it was found to be statistically significant.

**Conclusions:** it was concluded that the more intense Valsalva maneuvers would result in greater reductions in both middle cerebral artery blood flow velocity and cortical oxygenation, and that the reduction in oxygenation would be matched by an increased flow velocity in phase IV of the Valsalva maneuver.

**Keywords:** Female, Valsalva maneuvers, mean arterial blood pressure, Middle cerebral artery.

## INTRODUCTION

The Valsalva maneuver is commonly performed during everyday activities such as lifting, defecation and coughing, and is characterized by changes in intrathoracic

pressure that have a pronounced effect on venous return, cardiac output and blood pressures.<sup>[1]</sup> Phase I of the Valsalva maneuver is characterized by an increase in mean arterial blood pressure (MAP) at the onset of strain as the elevated intrathoracic pressure is translated to the arterial circulation; during phase IIa a reduction in atrial filling pressure decreases stroke volume with a baroreflex – mediated recovery in blood pressure, via an increased heart rate (phase IIb); phase III features a rapid decline in MAP as the strain is released and; phase IV has a rapid recovery and overshoot of MAP as the now restored cardiac output is ejected into a constricted systemic vasculature. <sup>[1,2]</sup> The Valsalva maneuver (VM) produces large and abrupt changes in mean arterial pressure (MAP) that challenge cerebral blood flow and oxygenation. <sup>[3]</sup> The abrupt reduction in MAP during phase III challenges the regulation of cerebral perfusion and can result in syncope even after brief 10s of Valsalva maneuver when standing <sup>[3]</sup>. Syncope occurs due to an acute reduction in cerebral oxygenation leading to unconsciousness. <sup>[4]</sup> The intrathoracic pressure perturbations during the Valsalva maneuver are translated to the cerebrospinal fluid such that increases in intracranial pressure (ICP) ensue, reducing transmural pressure in the cerebral arteries and thus flow. <sup>[5]</sup> Large changes in ICP potentially impair cerebral perfusion and have been used to induce occlusion. Whilst more intense Valsalva maneuver produce greater reductions in cerebral blood flow (CBF) velocity during Phase III <sup>[4]</sup>, it is not known whether these fluctuations in flow coincide with changes in oxygenation.

Various tissues display reactive hyperemic responses, such as skeletal muscle and skin in response to exercise. The brain also displays reactive hyperemic flow following injury <sup>[6]</sup>, stroke and surgical intervention. <sup>[7]</sup> Work in animals has shown that brief cerebral ischemia (5 s) can lead to a near-maximal hyperemic response. However, studies in healthy conscious humans exhibiting cerebral reactive hyperemia are scarce. Whilst a hyperemic response has been suggested during the phase IV response <sup>[8]</sup>, no concurrent beat-to-beat measures of CBF and oxygenation have been reported during a Valsalva maneuver.

## MATERIAL AND METHODS

Thirty young female participants were recruited for the study. Participants were informed of the likely risks and experimental procedures. Informed written consent was obtained from all the participants. A prior Ethical Approval was taken from Institutional Ethics Committee (IEC) of the BPS Govt. Medical College for women, Khanpur Kalan, Sonapat. All participants groups were free from disease and were not taking any medication. Participants were instructed to abstain from strenuous exercise,

alcohol and caffeine for at least 24hr before the experimental trial. A common familiarization session was arranged for the participants. During the familiarization session the participants were familiarized with all experimental procedures and equipment, including practicing Valsalva maneuvers (VMs).

During the experimental session each participant first stood for 5min, during which baseline measures were obtained, then completed a maximal VMs for 10 second. Following recovery, relative VMs of 30 and 90% of the maximal Valsalva pressure was performed for 10 s, the order of which was randomized between participants. These relative pressures were used to demonstrate graded cerebral blood flow velocity restriction. <sup>[3]</sup> Each VM was separated b 5 min or until values had returned to baseline. Participants were verbally instructed what pressure and duration to obtain, immediately before the performance.

### **Inclusion Criteria**

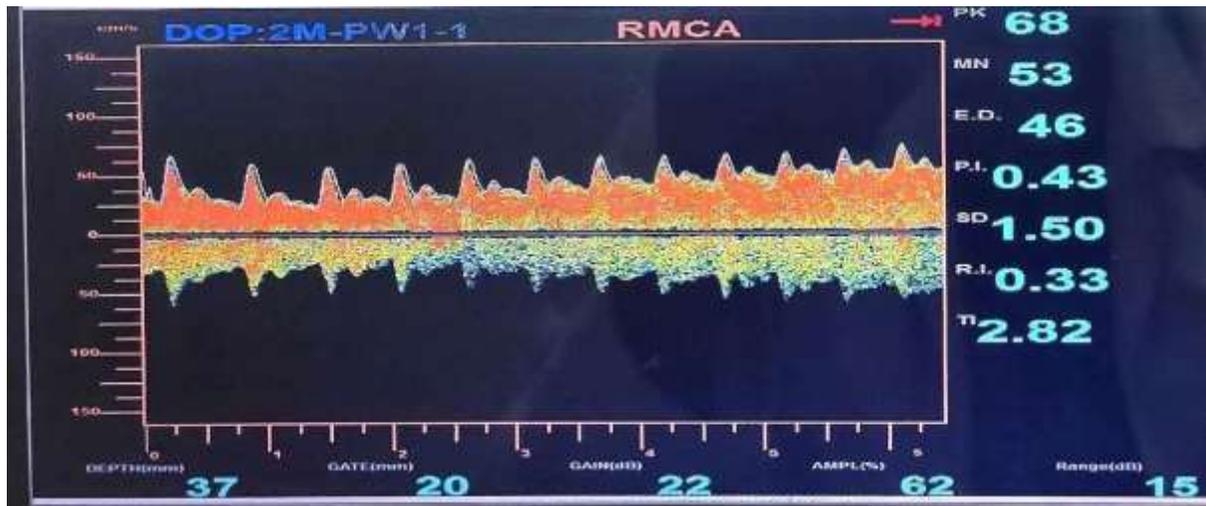
- a) Young Healthy Females

### **Exclusion Criteria**

- a) History of Diabetes
- b) History of Cardiopulmonary disease
- c) History of hypertension
- d) History of chronic respiratory illness
- e) Any history of vasovagal attack, fainting, syncope
- f) On any medications like anti hypertensive's.

Blood flow velocity was measured in the right middle cerebral artery (MCAv) using a 2-MHz Transcranial Doppler machine.<sup>[9]</sup> Transcranial Doppler sonography has proved to be a suitable non invasive technique for measuring cerebral blood flow (CBF) velocity in the large cerebral basilar arteries. Blood pressure was measured manually by digital sphygmomanometer during graded Valsalva maneuver (VMs). Mean blood flow velocity (MCAv<sub>mean</sub>) and mean arterial blood pressure (MAP) was calculated as the integral for each cardiac cycle divided by the corresponding pulse interval. An index of cerebral vascular conductance (CVCi) then was calculated via the equation  $MCAv_{mean}/MAP$ .

## Recording of the Transcranial Doppler



The statistical analyses of dependent variables were performed using a Student 't' Test. Data were assessed for approximation to a normal distribution and sphericity, with no corrections required. Linear regression analysis will be used to determine the correlation between the phase dependent changes in  $MCA_v$ , and MAP. All data will be analyzed using SPSS statistical software (Version 18), with a statistical significance set at  $P \leq 0.05$ . All data were presented as the mean  $\pm$  SD.

## OBSERVATION AND RESULTS

### Group statistics

Baseline- after VM, Baseline-90% VM, Baseline-30% VM, 90%-30% VM

Baseline - 90% VM corresponds to Phase-I of the VM (Peak Phase) and Baseline-after VM corresponds to Phase-III (nadir phase). Study variables are  $MCA_v$  mean, Systolic MCA, Diastolic MCA, MAP (Mean Arterial Pressure), CVC (Cerebrovascular Conductance).

All variables at the attainment of the "peak" for both the  $MCA_v$ mean and MAP phase I responses were used in the analysis (i.e., a data point for each individual peak). Time to peak was taken from the start of the VM to the  $MCA_v$ mean and MAP peaks independently. Each VM was analyzed for  $MCA_v$ mean and MAP times and magnitude of nadir (phase III), and time to recovery from the end of the strain. [23]

**Table no.1:-Changes in MCA<sub>v</sub> (Middle Cerebral Artery Blood flow Velocity) from baseline during Valsalva maneuver for 30% and 90% VM**

Variables	Groups	Mean	Std. Deviation	P-Value
MCA (Mean) MN	Baseline	55.60	11.77	0.001
	after VM	47.63	9.00	
	Baseline	55.60	11.77	0.107
	90 % VM	59.37	10.72	
	Baseline	55.60	11.77	0.52
	30 % VM	54.03	9.62	
	90 % VM	59.37	10.72	0.001
30 % VM	54.03	9.62		
Systolic MCA (PK)	Baseline	82.33	12.74	0.001
	after VM	75.67	11.95	
	Baseline	82.33	12.74	0.562
	90 % VM	84.07	11.32	
	Baseline	82.33	12.74	0.159
	30 % VM	78.30	8.66	
	90 % VM	84.07	11.32	0.001
30 % VM	78.30	8.66		
Diastolic MCA (ED)	Baseline	42.83	10.53	0.001
	after VM	34.27	7.59	
	Baseline	42.83	10.53	0.252
	90 % VM	45.63	9.81	
	Baseline	42.83	10.53	0.243
	30 % VM	39.97	9.84	
	90 % VM	45.63	9.81	0.001
30 % VM	39.97	9.84		

The mean difference between baseline ( $55.60 \pm 11.77$ ) and after VM ( $47.63 \pm 9.00$ ) is Statistically Significant ( $P \leq 0.05$ ) in MCA<sub>v</sub> mean. Similarly, the mean difference between 90% VM ( $59.37 \pm 10.72$ ) and 30% VM ( $54.03 \pm 9.62$ ) is statistically significant ( $P \leq 0.05$ ).

The mean difference between baseline ( $82.33 \pm 12.74$ ) and after VM ( $75.67 \pm 11.95$ ) is statistically significant ( $P \leq 0.05$ ) in Systolic MCA<sub>v</sub> (PK). Similarly, the mean difference between 90% VM ( $84.07 \pm 11.32$ ) and 30% VM ( $78.30 \pm 8.66$ ) is statistically significant ( $P \leq 0.05$ ).

The mean difference between baseline ( $42.83 \pm 10.53$ ) and after VM ( $34.27 \pm 7.59$ ) is statistically significant ( $P < 0.001$ ) in Diastolic MCA<sub>v</sub> (ED). Similarly, the mean difference between 90% VM ( $45.63 \pm 9.84$ ) and 30% VM ( $39.97 \pm 9.84$ ) is statistically Significant ( $P \leq 0.05$ ).

**Table no.2:-Changes in Mean Arterial Pressure (MAP) from baseline during Valsalva maneuver for 30% and 90% VM**

Variable	Groups	Mean	Std. Deviation	P-value
MAP (Mean Arterial Pressure)	baseline	84.97	15.10	0.410
	90%	82.47	10.31	
	baseline	84.97	15.10	0.013
	30%	76.52	9.74	
	baseline	84.97	15.10	0.001
	after	71.84	7.30	
	90%	82.47	10.31	0.014
	30%	76.52	9.74	

The mean difference between baseline ( $84.97 \pm 15.10$ ) and 30% VM ( $76.52 \pm 9.74$ ) is Statistically Significant ( $P \leq 0.05$ ) in MAP.

The mean difference between baseline ( $84.97 \pm 15.10$ ) and after VM ( $71.84 \pm 7.30$ ) is Statistically Significant ( $P \leq 0.05$ ) in MAP.

The mean difference between baseline 90% VM ( $82.47 \pm 10.31$ ) and 30% VM ( $76.52 \pm 9.74$ ) is Statistically Significant ( $P \leq 0.05$ ) in MAP.

**Table no.-3:-Changes of Cerebro vascular conductance (CVC) from baseline during Valsalvamanuever for 30% and 90% VM**

Variables	Groups	Mean	Std. Deviation	P-value
Cerebro vascular conductance (CVC)	Baseline	0.57	0.18	0.23
	after VM	0.61	0.18	
	Baseline	0.57	0.18	0.004
	90 % VM	0.70	0.12	
	Baseline	0.57	0.18	0.017
	30 % VM	0.66	0.13	
	90 % VM	0.61	0.18	0.01
	30 % VM	0.70	0.12	

The mean difference between baseline ( $0.57 \pm 0.18$ ) and 90% VM ( $0.70 \pm 0.12$ ) is statistically significant ( $P \leq 0.05$ ) in Cerebro Vascular Conductance (CVC).

The mean difference between baseline ( $0.57 \pm 0.18$ ) and 30% VM ( $0.66 \pm 0.13$ ) is statistically significant ( $P \leq 0.05$ ) in Cerebro Vascular Conductance (CVC).

The mean difference between 90% VM ( $0.61 \pm 0.18$ ) and 30% VM ( $0.70 \pm 0.12$ ) is statistically Significant ( $P \leq 0.05$ ) in Cerebro Vascular Conductance (CVC).

**Table no-4:-Comparison between Mean Arterial Pressure (MAP) and MCAvmean during Valsalvamanuever**

Group	Variable	Mean	Std. Deviation	P- Value
Baseline	MAP	84.97	15.10	0.001
	MCAvmean	50.43	20.08	
90%	MAP	82.47	10.31	0.001
	MCAvmean	50.36	15.49	
30%	MAP	76.52	9.74	0.001
	MCAvmean	54.03	9.62	
After	MAP	71.84	7.30	0.001
	MCAvmean	47.63	9.00	

The mean difference between MAP & MCAvmean ( $84.97 \pm 15.10$ ) is Statistically Significant ( $P \leq 0.05$ ) during baseline.

The mean difference between MAP & MCAvmean ( $82.47 \pm 10.31$ ) is Statistically Significant ( $P \leq 0.05$ ) during 90% VM.

The mean difference between MAP & MCAvmean ( $76.52 \pm 9.74$ ) is statistically significant ( $P \leq 0.05$ ) during 30% VM.

The mean difference between MAP & MCAvmean ( $71.84 \pm 7.30$ ) is statistically significant ( $P \leq 0.05$ ) after VM.

In Table-1, time to peak (Phase-I) corresponding to group statistics baseline-90% in all three variables MCAvmean, systolic MCA, Diastolic MCA is statistically not significant. In group statistics baseline-after VM (Phase-III) nadir phase in all three variables MCAvmean, systolic MCAv, Diastolic MCAv is statistically significant. In Table-2, Mean arterial pressure in group statistics baseline-90% (Phase-I) is not statistically significant but group statistics baseline-after VM (Phase-III) is statistically significant ( $P < 0.05$ ). Time to peak MCAvmean and peak MAP during Phase-I of the MV was unaffected by Valsalva pressure ( $P = 0.410$ ,  $P = 0.107$ ). Time to nadir (Phase-III) falling the VM for MCAvmean and MAP showed significant co-relation between intensity of the VM. In Table-3, Cerebrovascular conductance in group statistics baseline-90% (Phase- I) is significant and in group statistics baseline-after VM (Phase-III) is not significant. All variables in group statistics 90%-30% VM were statistically significant. In Table-4, comparison between MAP and MCAvmean of baseline, 90%, 30% and after VM were done and in all variables, it was found to be statistically significant.

## Discussion

Transcranial Doppler sonography of the basilar arteries has become a well-established method for measuring blood flow velocity since it was introduced in 1982.<sup>[10]</sup> We used Transcranial Doppler ultrasound as a surrogate for cerebral blood flow, which provides a measure of blood flow velocity rather than absolute flow. The change in flow velocity has been found to accurately reflect changes in absolute flow as long as conduit artery diameter is unchanged.<sup>[11]</sup>

In our study we found that across the range of graded Valsalva maneuver increase in Middle Cerebral Artery Velocity (MCAv) with graded Valsalva maneuver. resulted in a greater reduction in both MCA  $V_{\text{mean}}$  and MAP upon release of Valsalva maneuver in phase III . It is consistent with our hypothesis that the more intense Valsalva maneuver would lead to greater reduction in both MCA blood flow velocity and cortical oxygenation and that the reduction in oxygenation would be matched by an increased flow velocity in phase IV of the Valsalva maneuver. The intrathoracic pressure is rapidly translated to the cerebrospinal fluid at the onset of the Valsalva maneuver such that ICP rises <sup>[12, 13]</sup> and reduces the transmural pressure within the cerebral arteries. <sup>[5]</sup> The reduction in transmural pressure may restrain the passive dilation in response to the acute increases in cerebral perfusion pressure during phase I of the Valsalva maneuver and subsequently increases in MCAv are restrained. Furthermore, right atrial pressure increases linearly with expiratory pressure <sup>[14]</sup> and may attenuate the pressure difference across the cerebral circulation. The MAP response to Valsalva maneuver was found to be intensity dependent in phase III. The MCA  $v_{\text{mean}}$  response also matched this response to MAP in phase III. Despite similar increases in MAP during phase I and IV, the MCAv increase is greater during phase IV <sup>[1]</sup> where ICP would be expected to be declining to near baseline levels.<sup>[13]</sup> Other mechanisms of regulation, such as the autonomic nervous system, may operate during these latter phases (phase IV) of the Valsalva maneuver to regulate cerebral blood flow.<sup>[8]</sup> This shows that Valsalva maneuver both challenges and contribute to the regulation of cerebral blood flow. MAP and MCAV changes seen in phase III were dependent on intensity. more intense Valsalva maneuvers produce a greater reduction in cerebral blood flow velocity.<sup>[4]</sup> This rapid reduction in MAP is likely attributable to the passive effect of intrathoracic pressure on the arteries<sup>[1,15]</sup> and the refilling of the distended pulmonary vessels.<sup>[2]</sup> The elevated venous pressure during a Valsalva maneuver will increase cerebral blood volume<sup>[2,16]</sup> reduce venous outflow and contribute to the

reduction in MCAv. This reduced flow, however, will be partially mitigated via an increase in arterial oxygen extraction.<sup>[17]</sup> The brain demonstrates high-pass filter characteristics, with high frequency oscillations in MAP being translated to the cerebral circulation.<sup>[18]</sup> Whilst the increase in CBF during phase I may be restrained by the mechanical increase in ICP and subsequent reduction in transmural pressure.<sup>[5]</sup> changes in flow velocity only when conduit artery diameter is unchanged.<sup>[11]</sup> which appears to be true during moderate changes in MAP.<sup>[19]</sup> Further, the retest reliability has been shown to be strong during repeated VMs using Transcranial Doppler.<sup>[20]</sup> The Valsalva maneuver is the part of our everyday physiological activities and it causes changes in the cerebral hemodynamic, hence a detailed understanding of Valsalva maneuver may provide information to identify brain disease and their risk factors.

### SUMMARY

The Valsalva maneuver is a normal activity performed normally by every individual during every day physical activity (lifting, coughing etc.). During Valsalva maneuver intrathoracic pressure increases which causes changes in cerebrovascular perfusion. In our study we find that Valsalva maneuver is a very useful activity and it can be applied clinically in conditions where decreased cerebrovascular perfusion is needed. (Stroke, Embolism). We assessed the role of various parameters like Mean Arterial Pressure (MAP), Middle Cerebral Artery mean blood flow velocity (MCAv<sub>mean</sub>). Cerebrovascular Conductance (CVC) on graded Valsalva maneuver using Transcranial Doppler machine (2 - MHz). It was found that graded Valsalva maneuver would result in greater reduction in both middle cerebral artery blood flow velocity and cortical oxygenation and it can protect from brain injury. This information can be applied clinically and may be useful to prevent severe brain damage and injury.

### CONCLUSION

In our study we examined the cerebral hemodynamic response to graded Valsalva maneuver and we found that the more intense Valsalva maneuvers would result in greater reductions in both middle cerebral artery blood flow velocity and cortical oxygenation, and that the reduction in oxygenation would be matched by an increased flow velocity in phase IV of the Valsalva maneuver. So, Valsalva maneuver may protect the brain from hyper perfusion injury. The study is useful to understand the mechanism cerebral hyperemic responses may have potential implications for patient care under many clinical conditions of brain injury. The information obtained may be utilized for assessment and management of neurological disorders.

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