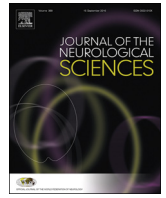




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Powered Air Purifying Respirator (PAPR) restores the N95 face mask induced cerebral hemodynamic alterations among Healthcare Workers during COVID-19 Outbreak

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ABSTRACT

Background and aim: COVID-19 pandemic has resulted in an unprecedented increased usage of Personal protective equipment (PPE) by healthcare-workers. PPE usage causes headache in majority of users. We evaluated changes in cerebral hemodynamics among healthcare-workers using PPE.

Methods: Frontline healthcare-workers donning PPE at our tertiary center were included. Demographics, comorbidities and blood-pressure were recorded. Transcranial Doppler (TCD) monitoring of middle cerebral artery was performed with 2-MHz probe. Mean flow velocity (MFV) and pulsatility index (PI) were recorded at baseline, after donning N95 respirator-mask, and after donning powered air-purifying respirator (PAPR), when indicated. End-tidal carbon-dioxide (ET-CO₂) pressure was recorded for participants donning PAPR in addition to the N95 respirator-mask.

Results: A total of 154 healthcare-workers (mean age 29 ± 12 years, 67% women) were included. Migraine was the commonest co-morbidity in 38 (25%) individuals while 123 (80%) developed de-novo headache due to N95 mask. Donning of N95 respirator-mask resulted in significant increase in MFV (4.4 ± 10.4 cm/s, $p < 0.001$) and decrease in PI (0.13 ± 0.12; $p < 0.001$) while ET-CO₂ increased by 3.1 ± 1.2 mmHg ($p < 0.001$). TCD monitoring in 24 (16%) participants donning PAPR and N95 respirator mask together showed normalization of PI, accompanied by normalization of ET-CO₂ values within 5-min. Combined use of N95 respirator-mask and PAPR was more comfortable as compared to N95 respirator-mask alone.

Conclusion: Use of N95 respirator-mask results in significant alterations in cerebral hemodynamics. However, these effects are mitigated by the use of additional PAPR. We recommend the use of PAPR together with the N95 mask for healthcare-workers doing longer duties in the hospital wards.

1. Introduction

During the rapidly emerging coronavirus disease 2019 (COVID-19) pandemic, there has been an unprecedented rise in the usage of

personal protective equipment (PPE) by healthcare workers [1]. Essentially, PPE comprises of N95 respirator, protective eyewear (goggles or face shield), gown and gloves [2]. Additionally, healthcare professionals deployed to the hospital areas where extremely high-risk

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aerosol-generating medical procedures are performed, it is imperative to use powered air-purifying respirators (PAPR), in addition to PPE [3]. Although, these equipment offer a high level of protection to healthcare professionals in fighting infections like COVID-19, it causes physical discomfort, resulting in poor compliance, especially when PPE is donned for prolonged duration [4,5].

Previous studies have shown that there is a significant increase in headache among frontline healthcare workers who used PPE for prolonged hours during Severe Acute Respiratory Syndrome (SARS) and COVID-19 outbreak [6,7]. One possible explanation for development of headache among PPE users was the external compression of sensitive facial skin and superficial nerves by face mask and its tight straps, especially when used for longer duration [6]. However, altered cerebral hemodynamics due to hypoxemia and carbon di-oxide (CO₂) retention have also been proposed to contribute to PPE-induced headache, especially for those who develop headache within minutes of wearing N95 respirator mask [8,9]. We evaluated cerebral hemodynamic changes during donning of N95 respirator mask alone as well together with PAPR among frontline healthcare workers during COVID-19 pandemic.

2. Methods

As a part of our hospital's infectious disease policy, all frontline workers were required to be mask-fitted and wear full PPE while managing patients with suspected and confirmed COVID-19 infection. A subgroup of the medical personnel involved in performing high-risk procedures like throat swabbing, endotracheal intubation or bronchoscopy underwent training for donning PAPR due to the heightened risk of aerosolization of COVID-19 virus.

2.1. Study population

This cross-sectional study was conducted between February and April 2020 on healthcare workers who underwent evaluation for headache related to the use of PPE at our tertiary institution [7]. The study was approved by institutional review board. All participants were at least 21 years old and agreed to participate in the study by signing an informed consent form. Baseline demographics, comorbidities, medical history and duration of N95 respirator use were prospectively recorded. All participants were mask-fitted for the 3 M® N95 respirator mask, certified by the National Institute for Occupational Safety and Health to filter out 95% of particles greater than 0.3 µm in size, protecting the user from inhalation of viral particles when worn appropriately. A subgroup of the participants were trained for additional donning of the PAPR (3 M® Versaflo® TR-300 series).

Participants with history of cerebrovascular disease, atrial fibrillation, intra- or extra-cranial arterial steno-occlusive disease were excluded.

2.2. Cerebral hemodynamics evaluation

We used transcranial Doppler (TCD) to monitor non-invasively, the cerebral blood flow changes in real-time [10–12]. In addition, TCD portability facilitated the test performance in individual wards, while adhering to the hospital-wide infection control and segregation policy during the current COVID-19 outbreak. Serial cerebral hemodynamic changes during the donning of PPE and PAPR in selected cases were assessed using TCD monitoring.

All TCD evaluations were performed by experienced and credentialed sonographers (CB, CSH), according to American Society of Neuroimaging recommendations [13]. After confirming the presence of a sufficient temporal acoustic window with 2-MHz diagnostic TCD (Sonara Viasys Inc., US), both middle cerebral arteries (MCA) were evaluated (depth 45–55 mm) and the side with better Doppler spectra was selected for further monitoring [14]. Patients with insufficient

temporal acoustic windows on both sides were excluded from the study. In order to maintain a constant insonation depth and angle, Spencer's head frame (Spencer Technologies, US) was used in all study participants for continuous monitoring of blood flow. We performed unilateral instead of bilateral MCA monitoring, since the latter was technically more challenging and time consuming especially when the participants moved or changed their head position during donning of N95 respirator and PAPR [15]. Continuous TCD spectra, for 1-min each, were recorded at baseline (breathing ambient air), 5 min after donning N95 respirator mask and 5 min after donning N95 respirator together with and PAPR. The 5-min time was chosen to avoid fluctuations in mean flow velocities (MFV) and pulsatility index (PI) due to anxiety and altered breathing pattern as well as obtain a steady state end-tidal carbon dioxide (ET-CO₂) level. TCD spectra were digitally recorded for later analysis, which was performed independently by a credentialed neurosonologist (VKS). Peak systolic (PSV) and end-diastolic (EDV) flow velocities were used to calculate MFV as $EDV + (PSV - EDV)/3$. PI was calculated as $PSV - EDV/MFV$ [11–13].

2.3. Monitoring other physiological parameters

ET-CO₂ was continuously monitored with a capnometer (TIDAL Wave Sp Model 715; Novamatrix, Wallingford, CT). A thin plastic tube was inserted from the sides of N95 respirator mask while ensuring the air seal. ET-CO₂ values at the time of TCD recordings (at baseline, 5-min after donning N95 respirator mask and 5-min after donning PAPR) were recorded.

2.4. Statistical analyses

Categorical variables are expressed by numbers (n) and percentages (%) and continuous variables as mean ± standard deviation (SD). The effects of N95 or PAPR exposure on cerebral hemodynamics were analyzed with the use of two-way repeated-measures analysis of variance (ANOVA). A p-value of less than 0.05 was considered as statistically significant. Statistical analyses were performed using SPSS statistical package program version 25.0 for Windows (SPSS Inc., 2003, Chicago, IL, USA).

3. Results

A total of 154 frontline healthcare workers agreed to participate in the study. Majority of them were female (n = 103, 66.9%) with mean age of 29.6 ± 12.1 years (Table 1). Migraine was the commonest comorbidity in 38 (25%) individuals while 123 (80%) participants reported de-novo headache due to the donning of N95 mask (Table 1).

Mean systolic and diastolic blood pressure at baseline were 116 ± 8 and 75 ± 6 mmHg, respectively. Mean heart rate at baseline was 68 ± 10 per minute. These values did not change significantly during the study. All participants underwent TCD monitoring at baseline and 5 min after donning N95 respirator mask. We did not

Table 1
Baseline characteristics of the study population (n = 154).

Variables	Values
Mean Age in years (SD)	29.6 (12.1)
Female gender, n (%)	103 (66.9)
Co-morbidities, n (%)	
Hypertension	3 (1.9)
Diabetes mellitus	0 (0.0)
Hyperlipidaemia	1 (0.6)
Pre-existing migraine	38 (24.7)
De novo headache	123 (79.9)
Coronary artery disease	0 (0.0)
Congestive heart failure	0 (0.0)
Chronic obstructive pulmonary disease	0 (0.0)

Table 2
Change in cerebral hemodynamic parameters after donning N95 respirator mask (n = 154).

Parameter	Baseline	N95	Absolute Change	Relative Change	p value
Mean MFV (SD) in cm/s	56.7 (18.2)	61.1 (17.0)	+ 4.4 (10.4)	+12.3% (29.8)	< 0.001
PI (SD)	0.92 (0.16)	0.79 (0.12)	-0.13 (0.12)	-13.3% (11.3)	< 0.001

MFV: mean flow velocity, PI: pulsatility index, SD: standard deviation.

encounter suboptimal acoustic window in our study participants.

3.1. Cerebral hemodynamic changes during donning N95 respirator mask

Mean MFV for MCA at baseline was 56.7 ± 18.2 cm/s, which increased to 61.1 ± 17.0 cm/s after wearing the N95 respirator mask ($p < 0.001$, Table 2). This was accompanied by corresponding reduction in PI from 0.92 ± 0.16 to 0.79 ± 0.12 ($p < 0.001$, Table 2). There was no statistically significant difference in MFV change between participants with history of pre-existing migraine and those without such history. Interestingly, compared to the those without de novo headaches, participants who developed de novo headaches ($n = 123$), MCA MFV showed a statistically significant increase after donning N95 respirator mask (62.3 ± 17.8 cm/s from 55.9 ± 18.1 cm/s at baseline; $p < 0.001$), accompanied by a decrease in PI (0.93 ± 0.13 at baseline to 0.79 ± 0.13 during donning of N95 respirator mask ($p < 0.001$),

3.2. Cerebral hemodynamic changes during donning N95 respirator mask and PAPR together

A subgroup of 24 (15.6%) participants underwent training for PAPR, in addition to the N95 respirator mask. During initial donning of N95 respirator, MFV increased from 54.5 ± 8.7 cm/s at baseline to 61.4 ± 8.2 cm/s ($p < 0.001$, Table 3) while PI decreased from 0.92 ± 0.06 to 0.81 ± 0.06 ($p < 0.001$, Table 3). After donning PAPR and N95 respirator mask together, MFV increased to 59.9 ± 8.8 cm/s from baseline ($p = 0.004$, Table 3), while PI remained similar at 0.91 ± 0.06 compared to baseline ($p = 0.694$, Table 3). Serial TCD findings in a representative participant are presented in Fig. 1.

For this subgroup, serial ET-CO₂ recordings showed an increase from baseline (37.3 ± 1.3 mmHg) to 40.4 ± 1.6 mmHg after wearing the N95 respirator mask ($p < 0.001$, Table 3). However, ET-CO₂ levels returned to the baseline values after donning PAPR (Table 3, Fig. 2). The serial changes in TCD parameters and ET-CO₂ were similar in participants who reported headache due to PPE as well those who did not.

4. Discussion

Our study shows that the use of N95 respirator mask results in significant alterations in cerebral hemodynamics. However, these effects are mitigated by the use of additional PAPR. Interestingly, the cerebral hemodynamic effects are dependent on the ET-CO₂ level changes during the donning of N95 respirator mask alone and together

Table 3
Cerebral hemodynamic parameters after donning N95 respirator mask alone together with powered air purifying respirator (PAPR) (n = 24).

Parameter	Baseline	N95 alone	Change ^a	P	N95 + PAPR	Change ^b	p
Mean MFV (SD) in cm/s	54.5 (8.7)	61.4 (8.2)	+7.0 (6.9)	< 0.001	59.9 (8.8)	+5.5 (8.4)	0.004
PI (SD)	0.92 (0.06)	0.81 (0.06)	-0.10 (0.04)	< 0.001	0.91 (0.06)	0.00 (0.04)	0.694
Mean ET-CO ₂ (SD) in mmHg	37.3 (1.3)	40.4 (1.6)	+3.1 (1.2)	< 0.001	37.3 (1.3)	0.0 (1.2)	1.000

MFV: mean flow velocity, PI: pulsatility index, SD: standard deviation, ET-CO₂: end-tidal carbon dioxide.

^a Absolute change between baseline and after donning N95.

^b Absolute change between baseline and after donning PAPR.

with PAPR.

In this study, we used TCD measurements of MFV and PI. These parameters are reliable and validated surrogate markers of cerebral blood flow and vascular tone [12,16–18]. Cerebral blood flow can be altered by the change in partial pressure of CO₂ (PaCO₂) in arterial blood, blood pressure (BP) and the rate of cerebral metabolism. Among these factors, PaCO₂ is the most important determinant of the vascular tone in intracranial circulation and a rise in PaCO₂ by 1 mmHg proportionately increases CBF by 3–6% [19]. We recorded TCD flow velocities, ET-CO₂ values and systemic blood pressure levels at baseline, during donning of N95 respirator mask alone as well as together with PAPR in a subgroup of our study participants. Although, we did not monitor the rate of cerebral metabolism, it is extremely unlikely for this variable to change significantly during 12–15 min of participants' involvement in our study.

TCD derived PI primarily measures the downstream cerebral vascular resistance and is dependent on overall compliance of the arterial wall as well as the surrounding brain tissue, probably mediated by the release of nitric oxide [20,21]. Accordingly, CO₂ induced arterial vasodilation would result in a decrease in PI [22]. Importantly, being a ratio, PI values are not altered by change in angle of insonation that may occur due to head movement during TCD monitoring. Our study documented a reduction in PI following donning of N95 mask, which was associated with a significant increase in ET-CO₂. Importantly, this decrease in PI was restored within 5 min of donning PAPR, which was accompanied by a proportionate correction in ET-CO₂. Thus, both N95 respirator mask and PAPR resulted in significant changes in the cerebral hemodynamic albeit in the opposite directions.

In a recent study on PPE donners, we described a high prevalence of headache [7]. While most of the participants reported de novo headaches, the headache severity and frequency worsened in those with pre-existing history of headache disorders. Although, most of the participants suffering from headache could mark the pressure points over face and scalp, suggestive of compression or irritation of skin and superficial nerves being responsible, at least in part, to their headaches. Our study demonstrates the contributory role of vasodilatation of intracranial vessels due to CO₂ build-up in causing headaches related to the PPE use. Perhaps, the N95 respirator mask expands the effective dead space volume for respiration due to the tight seal around the mouth and nose, which results in hypercapnia, as observed in our subgroup with ET-CO₂ monitoring [23]. Interestingly, donning of PAPR led to normalization of ET-CO₂ as well as cerebral hemodynamic parameters. We believe that the positive pressure generated by PAPR resulted in a relative hypoxemia by increased concentration of oxygen inside the hood and by positive pressure assisted exhalation. Although we cannot substantiate, this relative hypoxemia during PAPR could have upregulated the

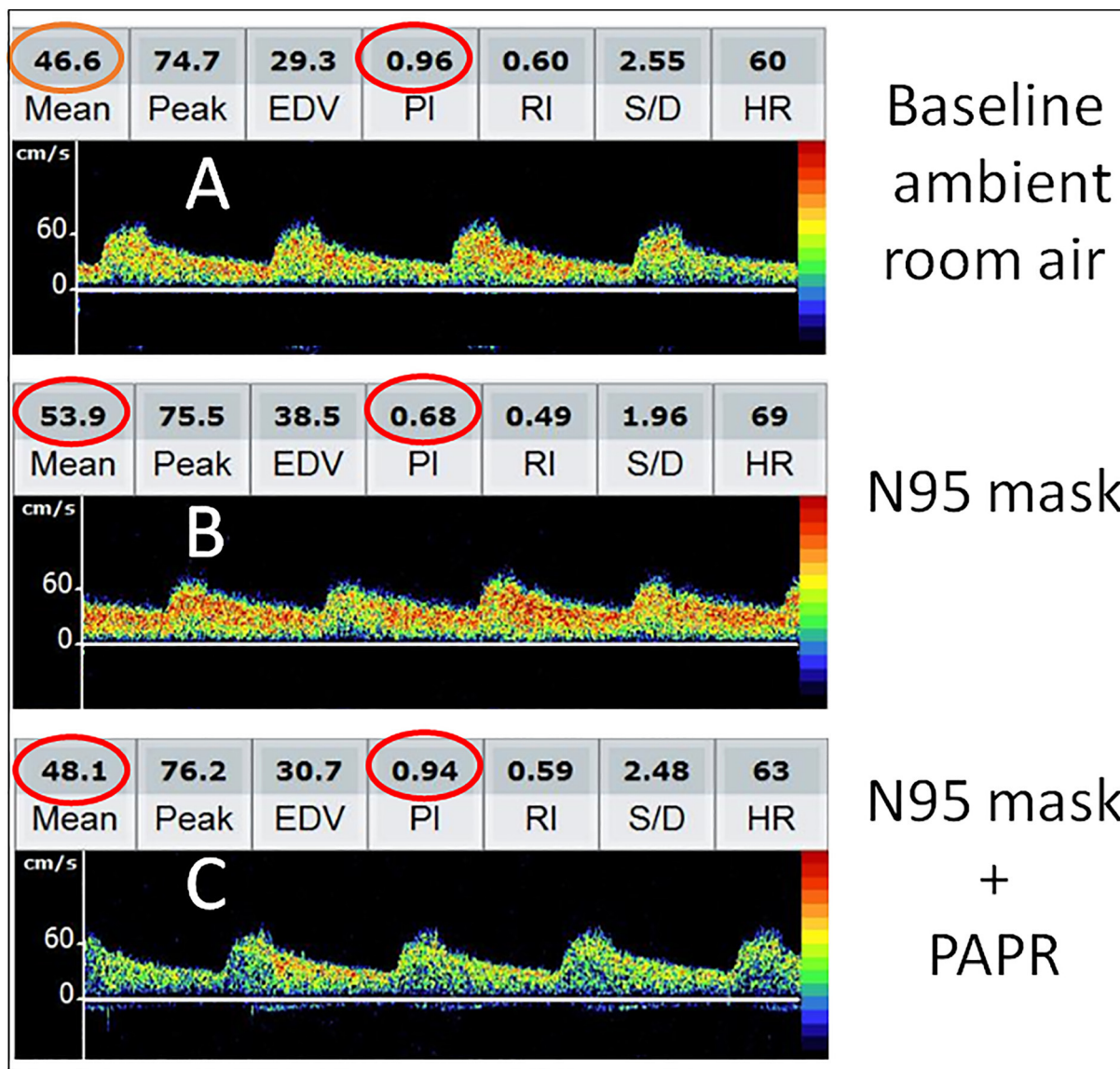


Fig. 1. Serial transcranial Doppler (TCD) changes during donning of N95 respirator mask alone and together with powered air purifying respirator (PAPR). While breathing ambient room air, Doppler spectra from right middle cerebral artery showed mean flow velocity (MFV) 46.6 cm/s and pulsatility index (PI) 0.96 (A). After donning N95 respirator mask for 5-minutes, MFV increased to 53.9 cm/s while PI decreased to 0.68 (B). However, both MFV and PI returned to near-baseline 5-minutes after donning PAPR and N95 respirator mask together (C).

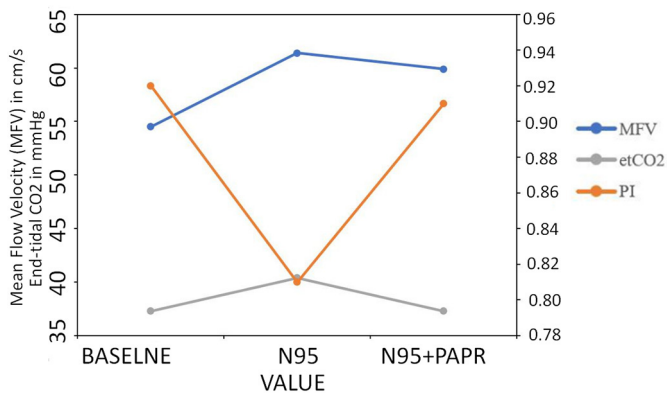


Fig. 2. Serial changes in mean flow velocity (MFV), pulsatility index (PI) and end-tidal carbon di-oxide (ET-CO2) during baseline (ambient room air), 5-minutes after donning N95 respirator mask alone and N95 respirator mask plus powered air purifying respirator (PAPR).

sympathetic activity while downregulating parasympathetic modulation. Interestingly, all participants reported the combined donning of N95 respirator mask and PAPR more comfortable as compared to the use of N95 alone.

We acknowledge certain limitations of our study. First, ET-CO2 was monitored only in a small subgroup of the study participants who donned PAPR in addition to the N95 respirator mask. However, getting a larger number of participants in this subgroup was difficult due to the strict hospital infection control guidelines about mixing of healthcare workers and safe-distancing policies. Also, PAPR training was provided only to the healthcare workers deployed in high risk hospital wards. Second, it is well known that ET-CO2 overestimates the CO2 levels as compared to arterial PaCO2 [24]. However, our aim was to evaluate the relative changes in cerebral hemodynamic parameters due to corresponding changes in ET-CO2 levels. Finally, changes in cerebral hemodynamic parameters were evaluated at 5 min after donning of N95 respirator mask and 5 min after donning additional PAPR. Whether, these changes are sustained or corrected by cerebral autoregulation remain unknown.

5. Conclusion

Our study shows that donning of N95 respirator alone or in combination with PAPR results in significant changes in cerebral hemodynamic parameters. The use of N95 respirator mask causes significant increase in MCA-MFV and ET-CO₂, coupled with reduction in PI. However, these changes, which probably contribute to the new onset headache by healthcare workers due to the wearing of N95 masks, are mitigated by the use of additional PAPR. Overall, PAPR maintains a favorable intracranial physiologically as compared to N95 respirator mask alone. Further large scale studies with prolonged monitoring are recommended to confirm our findings.

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