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Capillary carbon dioxide tension increases in hospital staff wearing filtering facepiece masks: a prospective crossover study

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In this prospective, single-centre, crossover study of 200 healthcare workers, an hour of wearing FFP2 or FFP3 masks while performing routine activities increased P_{cCO_2}, respiratory rate and subjective breathing effort https://bit.ly/3mtM31C

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Abstract

Background The COVID-19 pandemic has changed worldwide hygiene practices. In particular, the use of filtering face piece (FFP) masks markedly increased. Concerns have been raised regarding possible negative respiratory effects of wearing FFP masks. The aim of this study was to investigate gas exchange and subjective breathing effort in hospital personnel wearing FFP2 or FFP3 masks.

Methods In this prospective, single-centre, crossover study, 200 hospital workers were assigned to alternately wear FFP2 or FFP3 masks for 1 h during routine activities. Capillary blood gas analysis was performed to evaluate gas exchange while wearing the FFP masks. The primary end-point was the change in capillary partial pressure of carbon dioxide (P_{cCO_2}). In addition, capillary partial pressure of oxygen (P_{cO_2}), respiratory rate and subjective breathing effort were assessed at the end of each hour. Changes between time points and study groups were estimated using univariate and multivariate models.

Results P_{cCO_2} increased from 36.8±3.5 to 37.2±3.3 mmHg (p=0.047) and 37.4±3.2 mmHg (p=0.003) in individuals wearing FFP2 or FFP3 masks, respectively. Age (p=0.021) and male sex (p<0.001) were significantly associated with increased P_{cCO_2}. Similarly, the P_{cO_2} increased from 70.7±8.4 to 73.4 ±8.8 mmHg (p<0.001) and 72.8±8.5 mmHg (p=0.004) in individuals wearing FFP2 or FFP3 masks, respectively. Respiratory rate and subjective breathing effort increased significantly while wearing FFP2 and FFP3 masks (p<0.001 for all analyses). The order of wearing FFP2 or FFP3 masks did not significantly affect the results.

Conclusions An hour of wearing FFP2 or FFP3 masks increased P_{cCO_2} values, respiratory rate and subjective breathing effort in healthcare personnel performing routine activities.

Introduction

The COVID-19 pandemic has altered daily routines of healthcare personnel around the world in terms of hygiene and personal protective equipment (PPE) [1]. PPE has already been utilised during earlier epidemics to prevent medical staff from becoming infected [2]. In recent years, however, the widespread global use of PPE has reached levels not encountered before. This extensive use has subsequently led to discussions about the efficacy and possible side-effects of wearing PPE, and filtering face piece (FFP) masks in particular [3, 4].

Several studies evaluated the short-term influence of surgical masks and FFP masks on gas exchange or respiratory work [5–9]. In the largest study performed thus far, Medrzycka-Dabrowska *et al*. [7] evaluated capillary blood gas analysis in 110 nurses and paramedics before and after wearing PPE for 4 h. There was no significant difference in the blood gas values analysed. However, 29% of the participants reported negative symptoms such as fatigue or drowsiness. A limitation of the study is the non-uniform allocation of masks worn by the participants (29% FFP2 mask, 27% half-face mask with a FFP3 filter, 44% full-face mask with FFP3 filter). Most other studies listed used either end-tidal or trans-cutaneous methods to evaluate carbon dioxide concentrations.

In a pilot study, Sukul *et al.* [10] monitored exhaled breath profiles within mask space and reported an increase in hypercarbia and progressive deoxygenation in individuals wearing either surgical masks or FFP2 masks. Furthermore, the authors found secondary changes in haemodynamic parameters. Similarly, an increase in carbon dioxide levels in inhaled air was reported in children wearing either surgical masks or FFP2 masks [11]. Mapelli *et al.* [8] investigated the influence of masks on cardiorespiratory parameters at rest and during exercise in 12 healthy volunteers. The authors showed a moderate but significant decrease of spirometric and cardiorespiratory parameters. Additionally, in a very elaborate evaluation, Kisielinski *et al.* [12] described negative physical and psychological symptoms of wearing masks and have postulated possible consequences in many medical fields.

A recent review identified possible limitations of published studies: small cohorts, varying measurement tools for carbon dioxide concentrations and limited fit testing of the masks [13]. Taking these limitations into consideration, we developed a protocol to examine changes in gas exchange, respiratory rate and subjective breathing effort in hospital personnel wearing FFP2 or FFP3 masks during routine activities. Primarily, we evaluated the change in the capillary partial pressure of carbon dioxide (P_{cCO_2}) while wearing a FFP mask. Both changes caused by wearing the respective FFP mask and the difference between the mask types were studied.

Methods

This prospective crossover study was performed at the Medical University of Vienna between July 2021 and February 2022. Approval was obtained from the ethics committee of the Medical University of Vienna (EK1144/2021), and the study was registered at clinicaltrials.gov (NCT04980820). The study was conducted in accordance with the guidelines defined by the Declaration of Helsinki. The authors report no conflict of interest in relation to the manuscript. The research was supported by funds from the Department of Anaesthesia, General Intensive Care and Pain Medicine of the Medical University of Vienna.

Study design

A flow chart of the study is depicted in figure 1. Inclusion criteria were age ⩾18 years, vaccination against COVID-19 and signed informed consent. Exclusion criteria were pregnancy and breastfeeding.

After baseline measurement without wearing a mask for 10 min, participants received a certified FFP2 mask (model KLT01; Laianzhi, Zhongshan, China) or FFP3 mask (Model LP303; Laianzhi). Participants were alternately assigned to start with a FFP2 mask or FFP3 mask. Study personnel ensured correct fit of

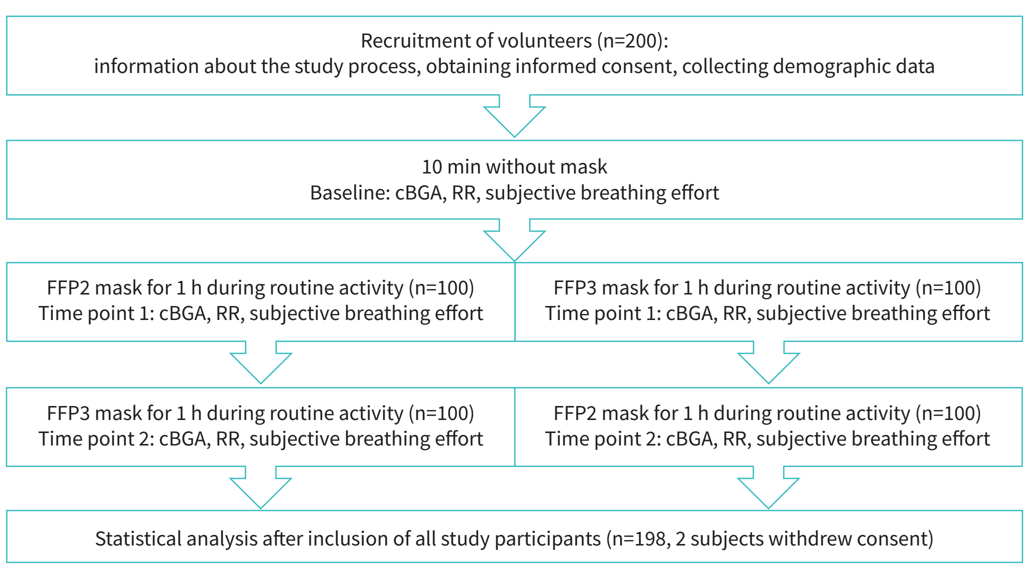

FIGURE 1 Flow chart of the study. cBGA: capillary blood gas analysis; RR: respiratory rate.

each mask. Individuals wore the mask for 1h while performing routine work (*e.g.* patient care, diagnostic examinations, surgical procedures). Blood gas analysis and data collection were then performed while individuals were still wearing the FFP mask (time point 1, TP1). Subsequently, individuals received a new FFP2 or FFP3 mask (whichever type had not been worn during the first phase), and all procedures were repeated (time point 2, TP2). This crossover design was chosen to exclude a change in the study parameters due to prolonged wearing of the mask. No time was specified for a possible "wash-out period" between exchange of masks.

Data collection

At all three measurements (baseline, TP1, TP2), a capillary blood gas analysis was performed, and the respiratory rate and subjective breathing effort were assessed. To evaluate the breathing effort, the study participants had to state how difficult it was for them to breathe (easy=1, rather easy=2, moderate=3, rather difficult=4, difficult=5). The blood sample was drawn from the fingertip with a 100-µL capillary tube (Radiometer Ltd, Krefeld, Germany). Analysis was performed with the blood gas analyser ABL800 FLEX (Radiometer Ltd). The following parameters were measured in the blood sample: P_{cCO_2}, capillary partial pressure of oxygen (P_{cO_2}), pH, base excess, haemoglobin, haematocrit, sulphur dioxide and bicarbonate (supplementary table S1).

Sample size calculation

Based on previous studies [14–16], we assumed P_{cCO_2} would increase from 40 to 43 mmHg while wearing FFP2 masks. With an α level of 0.05 and a power of 0.9, a total of 200 study participants needed to be recruited to achieve statistical significance (ANOVA with repeated measures – 3 time points).

Statistical analysis

Demographic data of the study participants are given descriptively. Continuous variables (*e.g.* age, weight, height) were summarised using mean, standard deviation, median, quartiles, minimum and maximum. Categorical variables (*e.g.* sex, profession) were summarised using absolute numbers and percentages. Descriptive statistics were calculated overall and separately for each condition (baseline, FFP2, FFP3).

Primary and secondary end-points

The difference in conditions (baseline, FFP2, FFP3) of the primary parameter P_{cCO_2} was first analysed using univariable linear mixed models accounting for the corresponding influence factor (condition, body mass index, age, sex, pre-existing cardiac or pulmonary disease, smoking) and proband number as random effect. To investigate the influence of the order (first FFP2 or first FFP3) on the effects of FFP2 or FFP3 masks on P_{cCO_2} (as compared to baseline), *i.e.* to evaluate overlapping compensatory efforts due to the crossover design between masks, a linear mixed model accounting for condition, order and the interaction between condition and order was performed. Influence factors being significant in the univariable models ($p<0.05$) were further investigated in a multivariable model. The secondary end-points P_{cO_2} and respiratory rate were analysed accordingly.

The secondary end-point "subjective breathing effort" was first analysed using univariable linear quantile mixed models (for the median) accounting for the corresponding influence factor (condition, body mass index (BMI), age, sex, pre-existing cardiac or pulmonary disease, smoking) and number of the study participant as random effect. To evaluate crossover effects, *i.e.* the influence of the order (first FFP2 or first FFP3) on the effects of FFP2 or FFP3 masks on subjective breathing effort (as compared to baseline), a linear quantile mixed model accounting (for the median) for condition, order, and the interaction between condition and order was performed. Influence factors being significant in the univariable models ($p<0.05$) were further investigated in a multivariable model.

All p-values <0.05 were considered as statistically significant. Sample size calculations were performed using www.statistikguru.de. All other analyses were performed using R, release 4.1.1. Note that no correction for multiplicity was performed. p-values of secondary end-points were interpreted only in an exploratory way.

Results

In total, 200 healthcare workers of the General Hospital of the Medical University of Vienna participated in the study. Two participants withdrew their consent after completing the study, resulting in 198 data sets in the final analysis. Of these 198 individuals, 78 were nurses, 74 doctors and 46 other medical staff (*e.g.* medical technical assistants, operating theatre staff). 76 participants were male and 122 female. 41 individuals were smokers, 13 of whom reported smoking >10 cigarettes per day. 24 participants reported pre-existing cardiac or pulmonary disease, while 12 were taking long-term medication. All other assessed demographic data of the study participants are given in table 1 and supplementary tables S2 and S3.

TABLE 1 Continuous demographic data of study participants

	Mean	Minimum	Maximum
Age years	34±10	20	61
Weight kg	72±13	43	106
Height cm	172±9	153	196
BMI kg·m^{-2}	24±4	17	37

Data are presented as mean with minimum and maximum. BMI: body mass index.

Primary end-point: P_{cCO_2}

In the univariable model, P_{cCO_2} increased significantly while wearing FFP2 masks ($p=0.047$) and FFP3 masks ($p=0.003$) as compared to baseline (figure 2a and supplementary table S4). No significant difference in P_{cCO_2} was observed between FFP2 and FFP3 masks ($p=0.300$). Both age ($p=0.021$) and male sex ($p<0.001$) were significantly associated with increased P_{cCO_2}. In contrast, BMI ($p=0.195$), pre-existing cardiac or pulmonary disease ($p=0.956$) and smoking ($p=0.280$) were not significantly associated with increased P_{cCO_2}. In the multivariable model accounting for condition, age and sex, all selected variables remained significant (supplementary table S5). Furthermore, the order of wearing FFP2 or FFP3 masks did not have a significant influence on P_{cCO_2} (interaction term for FFP2 masks compared to baseline −0.605 (95% CI −1.447–0.238), p-value 0.160; interaction term for FFP3 masks compared to baseline −0.269 (95% CI −1.115–0.577), p-value 0.195). One may therefore conclude that no significant overlapping compensatory efforts due to the crossover design were observed between FFP2 and FFP3 masks.

Secondary parameter: P_{cO_2}

In the univariable model, P_{cO_2} significantly increased while wearing FFP2 masks ($p<0.001$) and FFP3 masks ($p=0.004$) as compared to baseline (figure 2b and supplementary table S4). No significant difference in P_{cO_2} was observed between FFP2 and FFP3 masks ($p=0.366$). Similarly, BMI ($p=0.081$), age ($p=0.112$), sex ($p=0.081$), pre-existing cardiac or pulmonary disease ($p=0.604$) and smoking ($p=0.839$) were not significantly associated with a changed P_{cO_2} (supplementary table S6). Furthermore, the order of wearing FFP2 masks did not have an influence on P_{cO_2} (interaction term for FFP2 masks compared to baseline 1.679 (95% CI −1.060–4.418), p-value 0.230; interaction term for FFP3 masks as compared to baseline 0.679 (95% CI −2.058–3.416), p-value 0.627), *i.e.* no significant overlapping effects due to the crossover design were observed between FFP2 and FFP3 masks. No multivariable model was performed, since only condition showed a significant association with P_{cO_2} in the univariable analyses.

Secondary parameter: respiratory rate

In the univariable model, respiratory rate significantly increased while wearing FFP2 masks ($p<0.001$) and FFP3 masks ($p<0.001$; figure 2c and supplementary table S4). No significant difference in respiratory rate was observed between FFP2 and FFP3 masks ($p=0.916$). Both female sex ($p<0.001$) and pre-existing

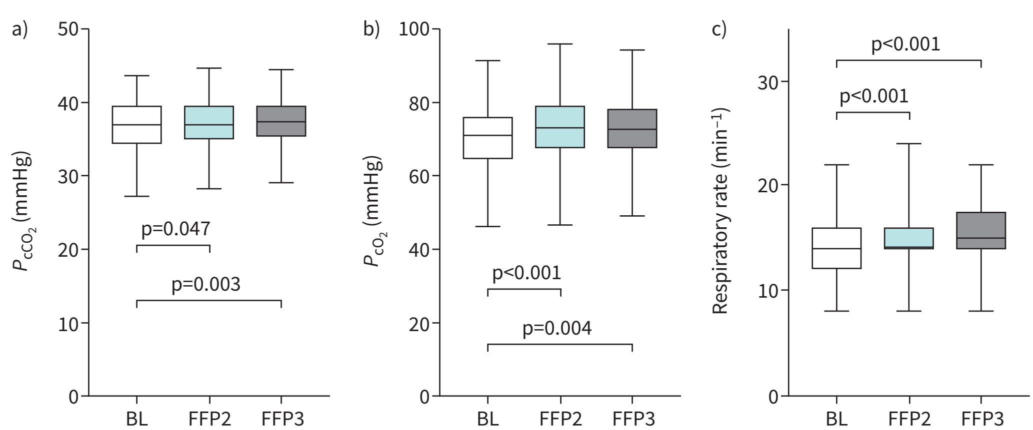

FIGURE 2 Box plots depicting changes in a) capillary partial pressure of carbon dioxide (P_{cCO_2}), b) capillary partial pressure of oxygen (P_{cO_2}) and c) respiratory rate. BL: baseline; FFP: filtering face piece (mask).

cardiac or pulmonary disease (p=0.012) were significantly associated with increased respiratory rate. In contrast, BMI (p=0.593), age (p=0.290) and smoking (p=0.508) were not significantly associated with increased respiratory rate. In the multivariable model accounting for condition, sex, pre-existing cardiac or pulmonary disease, all selected variables remained significant (supplementary table S7). Furthermore, the order of wearing FFP2 or FFP3 masks did not have a significant influence on respiratory rate (interaction term for FFP2 masks as compared to baseline −0.296 (95% CI −1.156–0.565), p-value 0.501; interaction term for FFP3 masks as compared to baseline −0.53 (95% CI −1.402–0.342, p-value 0.234).

Secondary parameter: subjective breathing effort

In the univariable model, the subjective breathing effort significantly increased while wearing FFP2 masks (p<0.001) and FFP3 masks (p<0.001, table 2). No significant difference in subjective breathing effort was observed between FFP2 and FFP3 masks (p=0.487). Body mass index (p=0.016), age (p=0.004) and smoking (p=0.023) were significantly associated with increased subjective breathing effort. In contrast sex (p=0.526) and pre-existing cardiac or pulmonary disease (p=0.085) were not significantly associated with increased subjective breathing effort. In the multivariable model accounting for condition, BMI, age and smoking, only condition and BMI remained significant (supplementary table S8). Furthermore, the order of wearing FFP2 or FFP3 masks did not have an influence on subjective breathing effort (interaction term for FFP2 masks as compared to baseline 0.052 (95% CI −0.252–0.149, p-value 0.605; interaction term for FFP3 masks as compared to baseline −0.025 (95% CI −0.274–0.224), p-value 0.843).

Discussion

In this study, we evaluated the effect of wearing FFP masks on gas exchange and subjective breathing effort in hospital personnel. We report an increase in P_{cCO_2} and P_{cO_2} after wearing a FFP2 or FFP3 mask for 1 h as compared to baseline measurements. In addition, respiratory rate and subjective breathing effort increased while wearing either FFP2 or FFP3 masks.

These results regarding the increase in P_{cCO_2} are comparable with other studies [17, 18]. Nafisah *et al.* [18] performed venous blood gas analysis on a total of 43 healthcare providers before and after 4 h of wearing an FFP2 mask. A significant increase in venous P_{CO_2} was observed. Age, sex and possible concomitant diseases had no influence. Similarly, Grimm *et al.* [17] reported an increase in P_{cCO_2} in 23 subjects wearing a surgical mask or FFP2 mask. In addition to blood gas analysis before and after exercise (20 min of bicycle ergometry), cognitive performance and haemodynamic parameters were recorded. Wearing a mask led to a slight increase in cardiovascular stress but did not affect cognitive performance.

In the present study, the P_{cO_2} also increased significantly when wearing either an FFP2 or FFP3 mask. These results differ from those in previously published studies. Nafisah *et al.* [18] found a small decrease in P_{O_2} in venous blood when wearing a FFP2 mask. In contrast, Grimm *et al.* [17] report a slight increase in P_{cO_2}. However, both authors do not elaborate on possible causes or the physiological background for their findings. A possible explanation for the increase in P_{cO_2} while wearing FFP masks in our study could be the increased breathing resistance due to the tight-fitting mask. Wearing face masks increases air flow resistance during tidal ventilation [19]. As the resistance is also encountered during expiration, the tight-fitting FFP masks could possibly create a slight positive end-expiratory pressure in the lungs. This positive end-expiratory pressure could potentially recruit some alveoli, increasing the area for gas exchange and consecutively raising the P_{cO_2}.

TABLE 2 Subjective breathing effort

Subjective breathing effort	BL %	FFP2 %	FFP3 %
1 (=low)	95.4	27.4	18.6
2	3.6	45.7	45.4
3	1.0	17.2	29.0
4	0	7.5	5.5
5 (=high)	0	2.2	1.6
Comparison	**FFP2 *versus* BL**	**FFP3 *versus* BL**	**FFP3 *versus* FFP2**
	<0.001	<0.001	0.487

BL: measurement after 10 min without mask; FFP2: measurement after 1 h wearing an FFP2 mask; FFP3: measurement after 1 h wearing an FFP3 mask. p-values for all group comparisons are provided (univariable model).

Wearing a FFP2 or FFP3 mask increased P_{cCO_2}, respiratory rate and subjective work of breathing in healthcare workers. However, the values are in a range in which the benefit of the mask predominates. The slightly increased respiratory rate in individuals wearing FFP masks might be explained by the increase in P_{cCO_2}. Increased levels of carbon dioxide in the bloodstream can increase respiratory rate, a physiological mechanism known as the hypercarbic respiratory drive [20]. Rhee *et al*. [21] also found increased carbon dioxide levels in the air breathed when wearing a mask. However, these values fell within the range set by the National Institute for Occupational Safety and Health for carbon dioxide concentration in the workplace. For patients with severe concomitant diseases, wearing a FFP2 mask can of course be a burden. Kogel *et al*. [22], for example, investigated the effect of a surgical or FFP2 mask on cardiopulmonary exercise capacity in 12 patients with heart failure. They found that wearing a FFP2 mask during spiro-ergometry reduced oxygen uptake and peak ventilation. Ramos-Campo *et al*. [23] investigated the effect of wearing a surgical or FFP2 mask during training sessions of 14 patients with sarcoidosis. Physiological and strength response during a resistance training session was similar in the subjects studied. Both authors concluded that the benefits outweigh the possible impairment caused by the mask.

In a recent study, Sukul *et al*. [10] observed a significant increase in end-tidal P_{CO_2} in adults wearing FFP2 masks over 30 min. Shallow breathing and higher inspiratory efforts were particularly present in older individuals wearing FFP2 masks, suggesting that wearing masks may be particularly challenging for this population. It is possible that existing respiratory issues or decreased respiratory muscle strength make it more difficult for older adults to tolerate the breathing resistance imposed by FFP2 masks, which could compromise compensation efforts. In our study, most individuals were younger than 60 years. Thus, comparability between studies is limited.

The strengths of our study compared to previous publications is the robust number of study participants and the crossover design. Limitations are the relatively short observation period of 1 h per mask and the lack of a wash-out period before donning the second mask. However, an adaptation of respiration and blood gas values can be assumed even during the time frame of 1 h and without a wash-out period. In order to find possible long-term effects, it would of course be necessary to conduct further studies. In addition, it is important to note that we have not used surgical masks in our study due to the mandatory use of FFP2 or FFP3 masks in Austrian hospitals during the pandemic. Therefore, the findings of this study may not be applicable to individuals wearing different types of face masks, especially considering that surgical masks represent one of the most used PPEs. Finally, it might be difficult to generalise the effects observed in this study to the general population, as the study participants were healthcare workers who were accustomed to wearing face masks during their daily work activities. Overall, it is important to consider individual factors such as respiratory health, mask type or level of physical activity when assessing potential effects of wearing a face mask on respiratory parameters in the general population. Further research is needed to understand fully the effects of wearing different types of face masks on respiratory function in various populations.

In summary, an hour of wearing FFP2 or FFP3 masks increased P_{cCO_2} and P_{cO_2} values, respiratory rate and subjective breathing effort in healthcare personnel performing routine activities. The reported changes are statistically significant, albeit minor, and it remains to be evaluated whether or not they are clinically or physiologically significant.

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