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Efficacy and feasibility of a novel semi-facial respirator with chitosan nanoparticles on the incidence of SARS-CoV-2 infection in healthcare professionals: randomized controlled trial

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Abstract

Background Evidence suggests that semi-facial respirators provide protection against contamination in high-risk environments, although the COVID-19 pandemic called for greater protection and viral inactivation capacity. Thus, the aim of this study was to investigate the efficacy of a novel semi-facial respirator containing chitosan nanoparticles, compared with a conventional N95 respirator on the incidence of laboratory-confirmed SARS-CoV-2 in healthcare professionals. The secondary outcomes were influenza infection, usability and comfort.

Methods Randomized controlled trial within a large public hospital (reference for COVID-19 patients) carried out between March 2021 and June 2023. We included 230 healthcare professionals exposed to SARS-Cov-2 and influenza, working in emergency departments, hospital wards, and intensive care units. Participants were assessed at baseline, after 10 days, and 21 days of follow-up. Researchers, participants, and outcome assessors were blinded to the allocated groups. Outcomes were analyzed by bivariate and multivariate comparisons using logistic regression. Crude (cOR) and adjusted odds ratios (aOR) were estimated, followed by 95% confidence intervals (CIs 95%). We adopted intention-to-treat (ITT) and complete-case (CC) analyses.

Results Baseline characteristics were considered homogeneous between groups, and usability and comfort were reported as excellent in both groups. Non-significant differences were found for all outcomes, both in the ITT and CC analyses. The incidence of COVID-19 and influenza were, respectively, cOR: 0.96 [CI95%: 0.21–4.42] and cOR: 1.25 [CI95%: 0.34–4.62]; and aOR: 1.08 [CI95%: 0.21–5.47] and aOR: 1.11 [CI95%: 0.17–7.01].

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Conclusions We found that the incidence of SARS-CoV-2 and influenza infections were similar between the new respirator compared to the conventional respirator. Furthermore, we observed that usability and comfort were similar and considered excellent for both respirators.

Trial registration Clinicaltrials.gov (NCT04490200, 29/07/2020).

Keywords Personal protective equipment, Healthcare professionals, COVID-19, Public health

Introduction

The pandemic caused by the novel coronavirus (SARS-CoV-2) forced health authorities around the world to adopt control measures such as physical or home isolation, mainly due to the ease of transmission and spread of the virus [1]. Another fundamental measure, especially in the context of healthcare professionals engaged in the care of infected patients, was wearing semi-facial masks or respirators, which have specific characteristics to contain certain types of particles [2].

Semi-facial respirators with N95 particle filters are recommended to reduce the transmission of infectious diseases. These respirators contain a type 2 filtering face-piece (FFP2) with 95% filtration capacity for solid, liquid or oil particles, and 98.5% filtration efficiency against bacteria [3]. However, previous studies suggested that N95 respirators have a reduced ability to filter smaller particles (0.1 to 0.3 μm) [4–7] such as SARS-CoV-2 viral particles, whose size ranges from 0.05 to 0.2 μm [8, 9]. Policy recommendations for wearing semi-facial respirators are based on protection against infection in high-risk environments. For instance, continuous wearing of N95 respirators resulted in significantly lower rates of clinical respiratory infection compared with surgical masks [10–12], or even similar protection against influenza infection [10, 13].

However, the high rate of contamination and spread of the SARS-CoV-2 virus has led to calls for increased protection. Accordingly, nanomaterials have been used for health applications, such as in protective equipment such as semi-facial respirators, to reduce particle permeability and favour a biocidal effect, thereby increasing their filtering capacity. Chitosan, a polysaccharide derived from the exoskeleton of crustaceans, can inactivate some viruses with negative surface charges and may act in viral adsorption due to its cationic nature [14]. Therefore, the use of chitosan in semi-facial respirators may represent a relevant application in the protection of healthcare professionals working in highly contaminated environments.

The present study aimed to investigate the clinical efficacy and feasibility of wearing a novel semi-facial respirator called VESTA, which contains chitosan nanoparticles in its filter layer. In a previous study [15], preclinical tests demonstrated that the new respirator did not present toxicity in culture cells. Additionally, the new respirator showed a significant greater capacity for viral inactivation

compared with the conventional respirator. These findings confirmed the biological plausibility of the new technology, pointing to promising applications as personal protective equipment (PPE), particularly important in the context of the pandemic caused by COVID-19.

Thus, the aim of this study was to investigate the efficacy of this new technology (novel respirator - VESTA) compared to a standard semi-facial respirator (N95), worn by health professionals who worked on the front lines of the fight against the pandemic in a large hospital in the city of Brasília, considering the primary outcome of incidence of SARS-CoV-2 infection. Secondly, the outcomes of influenza incidence and the usability and comfort of respirators were analyzed. It was hypothesized that the new technology would be superior to the conventional respirator in the primary outcome of interest.

Method

Study design

This is a randomized controlled clinical trial, composed of two parallel groups, carried out between March 2021 and June 2023. The protocol was prospectively registered at clinicaltrials.gov (NCT04490200), and the study was reported in accordance with the recommendations of the CONSORT Guidelines [16].

Setting

The study was carried out in a large 320-bed hospital in the city of Brasília, which was a referral center for patients with COVID-19. Health care personnel in the emergency departments, hospital wards, and intensive care units (ICU) were included. The study followed all the hospital's operational standards and procedures, with the aim of investigating professionals in their routine work of managing COVID-19 infected patients.

Participants

The population consisted of health care professionals potentially exposed to SARS-CoV-2 and influenza due to work activity and who worked in urgency and emergency departments, hospital wards, and ICU.

For inclusion, participants had to meet the following criteria: (1) age between 20 and 59 years; (2) full-time work (total workload greater than or equal to 20 h per week) in the hospital under study. If the participants worked at more than one site, they should have at least

80% of their weekly workload in the investigated hospital; (3) work at the emergency department, ICU, and other places with probable circulation of SARS-Cov-2 and other respiratory viruses; (4) present with negative clinical and laboratory results for SARS-Cov-2 and influenza infection at baseline.

Participants were excluded if they met any of the following criteria: (1) pregnant or breastfeeding women; (2) history of high-risk comorbidities for worsening COVID-19 (e.g., cardiac or respiratory diseases); (3) presence of heterogeneous facial anatomical characteristics that potentially caused incorrect wear of respirators (e.g., full beard, facial deformities or incompatible facial dimensions); (4) another chronic disease that, at the investigator's discretion, compromised participation and safety (e.g., hypertension or other comorbidity); (5) use of any substance or care equipment that interfered with normal respiratory function.

The study was approved by the Institutional Research Ethics Committee under CAAE protocol no. 39177620.5.0000.8093. All participants signed the Informed Consent Form (ICF).

Description of the interventions

After the randomization procedure and allocation to groups, all participants received VESTA semi-facial respirators (experimental group) or conventional N-95 respirators (comparison group) to be worn during their shifts and were followed for 21 subsequent days.

Upon delivery of the respirators, the participants received instructions for proper wear and care. In addition, all were instructed to wear one respirator per shift, with a maximal wear time of 8 h, following all standards and procedures established by the occupational safety department of the participating hospital. At the end of the shifts, everyone was instructed to discard the respirators, according to the manufacturer's recommendations. It is worth noting that the study did not affect the work routine of the research participants and followed all procedures and safety recommendations for the management and wear of N95 respirators adopted by the participating hospital.

Both respirators (experimental group and comparison group) were manufactured by the same company to ensure external visual similarity, standard of quality, and blinding of participants and researchers (i.e. so that they did not know which respirator each group would receive - concealed allocation). Further technical details about the respirators, and the translational pathway on the development can be found elsewhere [15, 17].

The respirators were distributed individually in small, plastic ziplock bags and grouped in opaque and sealed envelopes, forming kits with 10 units each. The entire process was conducted by an independent researcher

in a research laboratory with restricted access to minimize external interference and ensure a controlled and adequate environment for the kits. Each respirator and each kit were identified with alphanumeric labels specially developed to meet the randomization methodology, ensuring that the allocation of treatments was truly random. In this process, neither the participants nor the researchers could identify the contents of the packages or understand the codes. Pictures of the kits containing the masks of the control and experimental groups are available in the supplementary material (Supplementary Fig. 1). After the randomization and allocation process, the kits were distributed to the participants according to group allocation, and follow-up began in the study period (21 days).

Experimental group

The new respirator (VESTA) follows the same technical standards as N95 semi-facial respirators (class FFP2) currently in the national and international market, with adaptations related to technological innovation. One of the differences with this technology was the application of nanoparticles in its filter element, which is made of 50 gsm meltblown-polypropylene. Prior to the application of nanoparticles, the filter material was treated with an electrostatic charge and then followed with a deposition of chitosan nanoparticles.

Like the N95 respirator, the new VESTA respirator is fixed to the face by two side elastics, and the face seal is reinforced by a nose clip. The semi-facial mask is composed of three layers of filter material, the second layer being the filter element containing nanotechnology. The respirator is composed of two halves that open, forming a suitable enclosure for breathing. The side elastics ensure the pressure seal, and a nose clip ensures the front fit. The VESTA design met Brazilian recommendations, which require an adequate finish of the parts to avoid sharp edges and corners (RDC No. 356/2020).

Comparison group

The N95 FFP2 respirators on the market are manufactured with surgical non-woven fabric, as defined in national standards and resolutions (ABNT NBR 15052:2004 ANVISA RDC Resolution No. 356). Its filter element is formed by a layer of thin polypropylene fibers arranged randomly. The design of the standard respirator provides an adequate finish of the free parts to avoid sharp edges and corners.

Outcomes

Participants were evaluated at the following time points: (1) baseline (A0; pre-intervention); (2) after 10 days of follow-up (A1); (3) after 21 days of follow-up (A2). The

evaluations were performed by blinded evaluators, who were not aware of group allocation.

The primary outcome was the incidence of SARS-CoV-2 infection, confirmed by a laboratory using a RT-PCR test. The secondary outcomes were incidence of laboratory-confirmed influenza infection using RT-PCR and usability and comfort of the respirator. The RT-PCR test for SARS-CoV-2 and influenza was performed at time points A0, A1, and A2, or if the participant showed symptoms of COVID-19 or influenza. The test was performed by an experienced and trained researcher who also collected nasal samples from the participants. Synthetic fiber swabs (rayon) with plastic rods were used. The swab was inserted into the nostrils parallel to the palate and held in place for a few seconds and slowly removed. After collection, the swabs were placed immediately into sterile tubes containing 3 mL of viral transport medium.

The secondary outcome was the usability and comfort of the respirators applied at moments A1 and A2. The outcome was measured by self-report, using an 11-point Likert scale ranging from −5 (completely unsatisfactory), 0 (neutral), to +5 (completely satisfactory) [18]. The items covered in the scale included facial heat and sweat, wearing comfort, and ease of breathing.

Baseline measurements

Baseline measures were composed of demographic and occupational data (age, sex, marital status, education, professional classification, time working at the institution, workload, physical exercise, and sleep quality). The Work Ability Index (WAI) was used to assess the professional's perception of their current and future work ability. Finally, quality of life was measured using the Brazilian version of the EuroQol-5 Dimensions-3 Levels questionnaire (EQ-5D-3L).

The Work Ability Index (WAI) assesses workers' perception of their current and future work ability, health status and physical and mental capabilities. Thus, it predicts the conditions that lead to early loss of ability to work, early retirement, sick leave, and job loss [19]. In the present study, the short version of the WAI was used to measure the work ability of health care professionals, considering the two issues related to current and future work ability. Each participant's responses were based on a scale from 0 to 10, where 0 is "completely unable to work" and 10 is "work ability at its best". Thus, to measure the capacity for present and future work, the average score attributed by each participant in each of the questions was used.

The EuroQol-5 Dimensions-3 Levels (EQ-5D-3 L) questionnaire translated and validated for the Brazilian population was used to measure the quality of life of health professionals included in the study. The

EQ-5D-3 L consists of the EQ-5D descriptive system and the EQ visual analog scale (EQ VAS). In this questionnaire, five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) are evaluated with three possible answers for each, based on severity levels (I have no problems / some problems /extreme problems). The score ranges from 0 to 1 and represents an individual's degree of preference for a given health state, where 0 is the worst state and 1 is the best state [20]. Only the descriptive system was used in the study. A five-digit number representing the combination of a level of each of the five dimensions characterizes the health status of the individual. The EQ-5D-3 L defines 243 health states, each of which can be converted into a single EQ-5D-3 L score or index that incorporates social preferences for health status. Thus, the health status was converted into utility values.

Sleep quality was measured using three questions based on the Pittsburgh Sleep Quality Index [21]: During the last month, how many hours of sleep have you had per night? (this may be different from the number of hours you stayed in bed), where the answer is given in hours (whole numbers and fractions); 2. How do you rate the overall quality of your sleep during the last month? The answers ranged from "very good" to "very bad"; and 3. Do you have difficulty staying awake while working, eating meals, or engaging in social activities? The answer was "yes" or "no".

Sample size

The sample calculation was based on previous data from our pilot study. Our randomized controlled pilot trial was conducted from February to April 2021, following the same methodological procedures described within the clinical trial register. Sixty-three participants were randomized, of which 32 were allocated to the group that wore the new respirator and 31 to the group that wore the standard respirator. This new calculation was previously updated in the clinical trial register, to provide transparency. The calculation was performed considering a significance of 5%, statistical power ($1-\beta$) of 80%, and a minimum difference of Δ : 0.0665, given by the proportion of professionals who performed the test in the pilot study, and a sample variance s^2 : 0.17. Using these values, the sample calculation obtained was 303 professionals per group (total of 606 people). A correction was made for a finite population, considering the total number of health professionals working in the participating hospital (n : 1,968). After correction, the sample calculation indicated 262 participants per group (total of 524).

Randomization

Participants were randomized into one of the groups according to a table of random numbers, stratified by

sex and hospital department, which was implemented through a remote system via email. Based on the participants' IDs, sex, and date of birth, the team responsible for the allocation sent an email to the center, and the center replied automatically indicating the group to which each participant should be allocated, namely: respirator 1 and respirator 2. This procedure configured a hidden external allocation center based on codes associated with the mask kits, which were delivered to each participant. The researcher responsible for monitoring the allocation center did not know the objectives and purposes of the research.

Adverse events

We monitored possible adverse events (e.g., contact dermatitis, itching, etc.) during the follow-up, which were defined as unintended responses that occur during or after an intervention but are not necessarily caused by the trial intervention [22].

Data analysis

The outcomes of laboratory-confirmed COVID-19 incidence and laboratory-confirmed influenza incidence were analyzed using intention-to-treat analysis (ITT), including all randomized participants, regardless of protocol adherence, loss to follow-up, and lack of outcome data (primary analysis). Missing data for both outcomes were imputed using multiple imputation techniques. This method considered 25 predictor covariates in a logistic regression model for the imputation of missing data from these outcomes. For each imputed outcome, 5 imputed data sets were generated, and the results were obtained by combining these sets. Furthermore, sensitivity analyses were conducted in which the results were imputed in two scenarios: a best-case scenario (missing data for outcomes were imputed as negative) and a worst-case scenario (missing data for outcomes were imputed as positive). Secondary analysis, namely complete case analysis (CC), included only participants who completed the follow-up and who did not present lack of information regarding the analyzed outcomes.

Absolute and relative frequencies were calculated for categorical, median, and quartile variables (25%;75%) for quantitative variables, since the variables did not present a normal distribution. The Shapiro-Wilk test was used to verify data normality. To compare the quantitative variables, the Mann-Whitney U test was used, while for the qualitative variables, the Chi-square test or Fisher's Exact test were used. The significance level was set at 0.05.

To analyze the outcomes of laboratory-confirmed incidence of COVID-19 and laboratory-confirmed incidence of influenza after 21 days of follow-up, bivariate analyses were performed using logistic regression to estimate odds ratios (OR) with their respective 95% confidence

intervals. Secondary analyses were carried out to estimate adjusted ORs using logistic regression. For adjustments, covariates were inserted in the multivariate model that presented a value of $p < 0.10$ when the groups were compared (sex, marital status, and work at more than one site), complemented by two variables considered proxies of exposure intensity (profession and work sector). All statistical analyses were performed using Statistical Packages for the Social Sciences (SPSS®), version 22.0.

Results

A total of 258 participants were assessed for eligibility. Of these, 28 were excluded resulting in a total of 230 participants who were randomized between the experimental group (n: 112) and comparison group (CG; n: 118). Details are presented in Fig. 1.

The primary outcome could not be evaluated in 31 participants (13 in the GExp and 18 in the CG), due to withdrawal from participation in the study, vacation, change of workplace, and positive result as reported by the participant, of a COVID test performed outside the laboratory used by the study.

We reported two adverse events, which were deemed not to have been caused by wearing the investigated semi-facial respirators (one participant of the CG reported coryza symptoms, minor eye swelling, and sneezing; and one participant of the CG reported hoarseness and coryza symptoms). No adverse events were reported in the GExp.

Table 1 shows the characteristics of the participants at baseline, broken down according to group allocation. Two variables (marital status and work at more than one site) were considered different between groups. The other variables showed a homogeneous distribution among the groups, indicating that the randomization was successful.

Data related to the perception of respirator usability are presented in Table 2. Usability was considered excellent, and no significant differences were found between the groups when all usability components were compared, both at 10 days and at 21 days of follow-up.

Table 3 shows the results of the incidence of COVID-19 and incidence of influenza in the 21 days of follow-up, according to the type of analysis (ITT and complete cases). The analyses did not reveal a significant difference for either outcome in the ITT analysis or in the complete case analysis. The ITT analyses were more precise and showed point values close to zero, and the complete case analyses indicated specific ORs with greater magnitude, but showed imprecision, as evidenced by the confidence intervals. Supplementary Table 1 presents a sensitivity analysis in which outcomes were imputed under two scenarios: a best-case scenario (missing outcomes were imputed as negative) and a worst-case scenario (missing outcomes were imputed as positive). The results

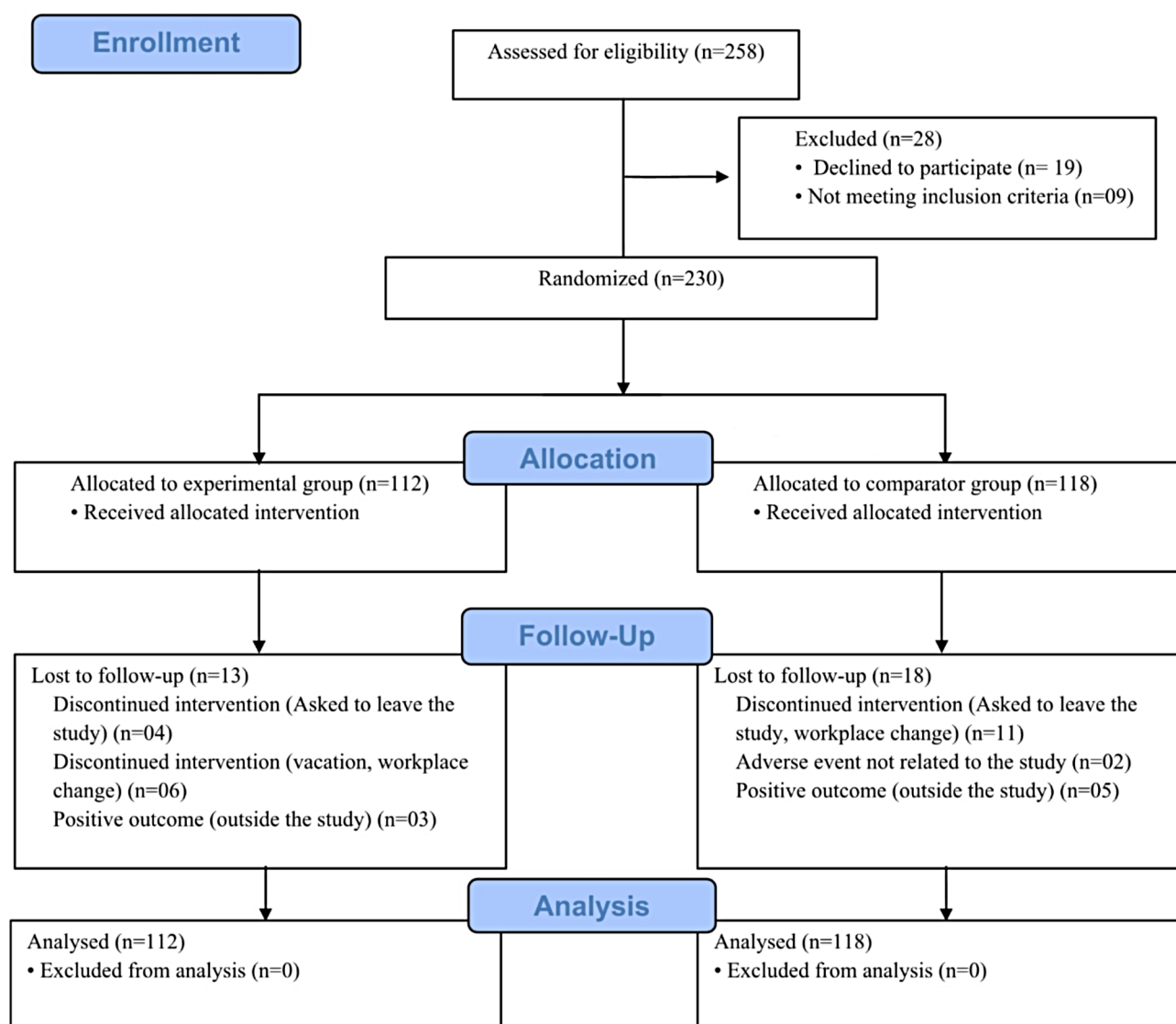


Fig. 1 Study flow chart

corroborate those presented in Table 3 and indicate that there was no statistically significant association in either scenario.

Discussion

This study aimed to investigate the effectiveness of a new semi-facial respirator composed of nanotechnology (i.e., VESTA respirator), compared to a conventional N95 respirator, in healthcare professionals who worked on the front line of the fight against the pandemic. Our findings demonstrated that the incidence coefficients of SARS-CoV-2 and influenza infection were similar between the groups. Additionally, we found that both respirators presented excellent usability and comfort, as self-reported by the participants.

The mean age of the healthcare professionals included was 40 years, similar to previous studies [23, 24] that had age groups between 31 and 40 years of age. We found that most participants were female and were nursing technicians and nurses. This finding is similar to previous studies [23–25] and was expected, considering that in Brazil, most nursing professionals are female [26]. This finding is also consistent with a World Health Organization (WHO) survey conducted in 104 countries, in which approximately 70% of the health workforce was shown to be composed of women [27].

We found no significant differences between the group that wore the new respirator compared to the standard respirator regarding the chances of infection by SARS-CoV-2 and influenza. It is also noteworthy that there was an imprecision as indicated by wide confidence intervals.

Table 1 Characteristics of participants at baseline according to allocation group (experimental – GExp and comparator group – CG)

Characteristics	GExp n = 112	CG n = 118
Sex - f (%)	29 (25.89)	19 (16.10)
- Male	83 (74.11)	99 (83.90)
- Female		
Age - MD (IQR)	42.00 (32.00–51.00)	43.00 (37.00–51.25)
Race/skin color - f (%)	47 (41.96)	35 (29.66)
- White	50 (44.64)	65 (55.08)
- Brown	14 (12.50)	16 (13.56)
- Black	0 (0.00)	1 (0.85)
- Asian	1 (0.89)	1 (0.85)
- Not stated		
Marital Status - f (%)	43(38.39)	61(51.69)
Married	69(61.61)	57(48.31)
Single		
Occupation f (%)	48 (42.86)	61 (51.69)
- Technician	27 (24.11)	29 (24.58)
- Nurse	11 (9.82)	5 (4.24)
- Physical Therapist	6 (5.36)	6 (5.08)
- Medical Doctor	20 (17.86)	17 (14.41)
- Other		
Education - f (%)	1 (0.89)	1 (0.85)
- Primary	12 (10.71)	9 (7.63)
- Secondary	99 (88.39)	108 (91.53)
- Tertiary		
Area of Employment - f (%)	41 (36.61)	45 (38.14)
Others	35 (31.25)	36 (30.51)
Hospital Ward	25 (22.32)	33 (27.97)
Emergency	11 (9.82)	4 (3.39)
Intensive Care Unit		
Works at more than one site - f (%)	27 (24.11)	43 (36.44)
- Yes	85 (75.89)	75 (63.56)
- No		
Work Hours - f (%)	26 (23.21)	34 (28.81)
- < 40 h/week	86 (76.79)	83 (70.34)
- ≥ 40 h/week	0 (0.00)	1 (0.85)
- Not stated		
COVID-19 Vaccine - f (%)	112 (100.00)	115 (97.46)
- Yes	0 (0.00)	3 (2.54)
- No		
COVID-19 History - f (%)	86 (76.79)	88 (74.58)
- Yes	25 (22.32)	30 (25.42)
- No	1 (0.89)	0 (0.00)
- Not stated		
Influenza Vaccine - f (%)	52 (46.43)	63 (53.39)
- Yes	60 (53.57)	54 (45.76)
- No	0 (0.00)	1 (0.85)
- Not stated		
Quality of Life (utility) - Mean (SD)	0.79 (0.74–1.00)	0.79 (0.74–1.00)

Table 1 (continued)

Characteristics	GExp n = 112	CG n = 118
Work Ability	8.00	8.00
- Current - MD (IQR)	(8.00–10.00)	(8.00–9.00)
- Future - MD (IQR)	8.00 (8.00–9.00)	8.00 (8.00–9.00)
Overall Sleep Quality - f (%)	14 (12.50)	22 (18.64)
- Very good	59 (52.68)	55 (46.61)
- Good	29 (25.89)	31 (26.27)
- Poor	10 (8.93)	9 (7.63)
- Very poor	0 (0.00)	1 (0.85)
- Not stated		

MD: Median; IQR: Interquartile range; SD: Standard deviation

Previous studies have suggested that semi-facial respirators (i.e., N95) were deemed to be effective in preventing respiratory viruses and bacterial infections, as well as maintaining protection against coronaviruses in healthcare workers [28–30]. In addition, policy recommendations showed that wearing a face mask or semi-facial respirator in indoor public settings was associated with lower adjusted odds ratio of COVID-19 contamination (OR: 0.44; 95%CI: 0.24;0.82) [31]. Nevertheless, some studies highlighted limitations of N95 respirators in protection against small virions [5], which might partially explain our findings. As SARS-Cov-2 particles are much smaller than other known viruses, it is possible to assume that the nanoparticle filter element may not have been sufficient to highlight minimally significant differences compared to the conventional respirator. However, the imprecision of the findings points to the fact that the statistical power of the study was low and did not favor definitive conclusions regarding the clinical efficacy related to COVID-19 and influenza infection, even though pre-clinical tests and previous studies have demonstrated the potential of viral inactivation provided by nanoparticles. Some aspects could explain the imprecision, such as the small number of events (COVID-19 and influenza infection) and the design of a randomised controlled trial in a real-world public hospital setting, which implies uncontrolled variables that may have affected the results. Although we used ITT and CC analyses to mitigate these effects, residual variability may have contributed to the wide confidence intervals. Therefore, we assume that semi-facial respirators are a valuable component of personal protective equipment for healthcare professionals working in hospital environments, although it must be accompanied by other infection control practices to ensure maximum protection of this population.

This clinical trial was designed with high methodological rigor to reduce the risk of bias. Initially, we verified homogeneity between the groups considering the baseline variables, which demonstrates that the randomization process was successful. This aspect is relevant

Table 2 Respirator usability, according to allocation groups, measured at time points A1 and A2 (10 and 21 days of follow-up, respectively)

Usability and comfort items	GExp MD (IQR)	CG MD (IQR)	p-value ^a
Heat and sweat	3.00 (1.00–4.00)	3.00 (1.00–4.00)	0.352
A1	4.00 (2.00–4.00)	3.00 (1.00–4.00)	0.246
A2			
Easy to breathe	4.00 (3.00–5.00)	4.00 (2.00–5.00)	0.988
A1	4.00 (3.00–5.00)	4.00 (3.00–5.00)	0.156
A2			
Easy to talk	4.00 (3.00–5.00)	4.00 (3.00–5.00)	0.670
A1	4.00 (3.00–5.00)	4.00 (3.00–5.00)	0.369
A2			
Itchiness	4.00 (2.00–5.00)	5.00 (1.00–5.00)	0.954
A1	5.00 (2.75–5.00)	5.00 (3.00–5.00)	0.943
A2			
Comfort around the ear	5.00 (3.00–5.00)	4.00 (3.00–5.00)	0.551
A1	5.00 (3.00–5.00)	5.00 (3.00–5.00)	0.340
A2			
Comfort around the clip/nose	4.00 (3.00–5.00)	4.00 (3.00–5.00)	0.538
A1	4.00 (3.00–5.00)	4.00 (2.00–5.00)	0.180
A2			
Maintenance of mask position	4.00 (4.00–5.00)	4.00 (3.00–5.00)	0.089
A1	4.00 (3.00–5.00)	4.00 (3.00–5.00)	0.813
A2			
Seal	5.00 (4.00–5.00)	5.00 (4.00–5.00)	0.608
A1	5.00 (4.00–5.00)	5.00 (4.00–5.00)	0.275
A2			
Overall comfort	4.00 (3.00–4.00)	4.00 (2.50–4.00)	0.246
A1	4.00 (3.00–5.00)	4.00 (3.00–4.00)	0.442
A2			

^aMann-whitney test; MD: Median; IQR: Interquartile range**Table 3** COVID-19 and Influenza A and/or B infection according to crude odds ratio and adjusted according to intention-to-treat (ITT) and complete case (CC) analyses

Outcome	Gexp Events/total	CG Events/total	Crude OR (CI95%)	Adjusted OR ^a (CI95%)
Incidence of COVID-19				
ITT analysis	8,4/112 ^b	9,2/118 ^b	0.96 (0.21–4.42) ^b	1.08 (0.21–5.47) ^b
CC analysis	3/99	1/100	3.09 (0.31–30.26)	1.75 (0.11–27.07)
Incidence of Influenza				
ITT analysis	7/112 ^b	6/118 ^b	1.25 (0.34–4.62) ^b	1.11 (0.17–7.01) ^b
CC analysis	1/96	1/96	1.00 (0.62–16.22)	1.00 (0.29–34.38)

^a Adjusted using binary Logistic Regression^b Results generated by combining five data sets produced with the multiple imputation technique

OR: odds ratio; CI95%: 95% confidence interval

^c Gexp=Experimental group; CG=Comparison group

because it has long been recognized that randomization is a key aspect of clinical trials, ensuring unbiased comparisons between groups and avoiding selection bias [32]. In addition, the researchers responsible for monitoring, the participants, the outcome evaluators, and the researchers responsible for data analysis were blinded to group allocation. This is an important characteristic, as the adequate implementation of blinding in clinical trials reduces the chance of bias, such as the way investigators approach eligible participants and how they are assigned

to groups, thereby reducing the chance of selective bias [33]. Finally, it is noteworthy that the study was carried out in actual work conditions of healthcare professionals at a large reference hospital in the region for the treatment and management of patients affected by COVID-19. In this sense, it can be stated that our study was akin to a pragmatic clinical trial, providing data applicable to real-life practice, such as healthcare professionals working in hospital environments [34]. Taken together, this study demonstrates internal and considerable external

validity, provided by the methodological control of biases and reality of the participants, which guarantees confidence in the results.

However, there are several limitations that need to be highlighted. Initially, the recruitment process of participants was greatly influenced by the loosening of restrictions arising from the pandemic, especially in the second half of 2022. This may have influenced participant interest and adherence, and therefore the sample size we could achieve, making our study underpowered. We speculate that the professionals were dealing with burnout, which explains the non-adherence to the study and the evaluation process during the follow-up period. This is relevant because in several regions of Brazil, including the participating hospital, healthcare professionals were strongly influenced by the excessive workload and great demand imposed by the pandemic on the health system [35].

It is worth noting that we decided to make one of the inclusion criteria more flexible to include participants who worked at more than one site. This criterion was chosen to ensure that the study was close to the real working conditions of these professionals. The fact that a percentage of participants worked at more than one site may have increased the likelihood of external exposure and reduced adherence and interest in participating in the clinical trial. Thus, the possibility of community-acquired infection cannot be completely excluded. However, we expected that any out-of-hospital infections should have been equally distributed between the groups as a result of the randomisation process. Finally, it is worth noting that most professionals were up to date with the vaccination schedule for COVID-19. With the advancement of the vaccination process throughout 2022 and prioritization of vaccination of healthcare professionals, we assume that the low incidence of the primary outcome may have been influenced by the vaccination status of the participants, which may have made it impossible to observe significant differences between the groups evaluated. We planned to monitor participants' adherence to the daily use of the semi-facial respirators in a diary. However, due to a low response rate from participants, we decided to exclude this information, resulting in a protocol deviation.

When analyzed together, the findings of this clinical trial and preclinical tests [15] show that, from a feasibility perspective, the new respirator has the potential to be adopted as a personal protective equipment (PPE) for healthcare professionals. Although the performance of both respirators was similar in all outcomes studied, a low incidence of COVID-19 and influenza infection was observed in participants, and both respirators demonstrated excellent ease of use and comfort.

It is also worth noting that in preclinical testing, the new respirator (VESTA) was superior to the conventional

respirator in terms of tear resistance and antibacterial and antiviral activity. In addition, the new respirator presented similar standards of aerosol penetration, breath resistance, and flammability required to be considered a safe respirator for healthcare by the Brazilian National Health Surveillance Agency (ANVISA) [15]. This allows us to hypothesize that, in a scenario with a larger sample size and a higher incidence of respiratory viruses, such as coronavirus, the new respirator would probably show superiority. However, this hypothesis needs to be confirmed in future studies. Although the data set was limited, preventing precise comparisons of efficacy, our results, when considered with all the available evidence, including previously published studies by our group, suggest that the new respirator may be a viable PPE option at the discretion of health managers and professionals.

Conclusion

Our findings demonstrated that the risk of acquisition of SARS-Cov-2 and influenza was similar among participants who wore the new semi-facial respirator compared to the conventional respirator. In addition, we found that all items related to ease of use and comfort were similar and considered excellent for both respirators.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12879-024-09966-x>.

Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

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Author contributions

AMAK, MFFR: Conceptualization, Data curation, Investigation, Methodology, Supervision, and Writing – original draft; SB: Conceptual review about research – Writing review and editing; JAMV, JDGS, MLBC, RH, GUSL, MULF, IRZ, SSRFR: Conceptual review about research – Writing review and editing; HMP, RLC: Conceptualization, Data curation, Investigation, Methodology, Supervision, and Writing – original draft.

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Data availability

All relevant data are within the paper and its Supporting Information files.

Declarations

Ethics approval and consent to participate

The study was approved by the Institutional Research Ethics Committee (University of Brasília) under CAAE protocol no. 39177620.5.0000.8093. All participants signed the informed consent form.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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