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CLINICAL TRIAL REPORT

A Novel Supraglottic Suction Device in Mechanically Ventilated Patients: A Randomized Controlled Trial

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Objective: To evaluate the efficacy and safety of the SUPRAtube innovation device in preventing ventilator associated events and fluid accumulation in the supraglottic region in patients receiving mechanical ventilation (MV) through orotracheal tubes.

Methods: Multicenter, controlled, randomized, parallel, open-label clinical trial with a 1:1 allocation ratio of MV patients compared the use of the SUPRAtube elastomeric device with standard care and aspiration techniques. A series of computer-random numbers and centralized allocation with sealed envelopes were used.

Setting: Adult patients (n=108; mean age: 63 yrs, range: 19–85) hospitalized in intensive care units of two centers, the Cardiovascular Foundation of Colombia and the International Hospital of Colombia (Santander, Colombia), were included. All patients received MV through orotracheal tubes, were hemodynamically stable, had upper airway integrity according to fiberoptic bronchoscope findings, and had basic coagulation tests within acceptable risk criteria.

Interventions: Comprehensive standard of care, including preventive strategies, medical therapy, positive pressure MV, and routine procedures for management of oropharyngeal and pulmonary secretions (humidification, patient mobilization, and airway suctioning), was compared with the standard of care plus continuous supraglottic suction with the new SUPRAtube device.

Results: The study period reached five days before extubation (media 85±7 hours). The weight of the aspirated content was 415 g (P25;P75: 396;536) in the control group and 624 g (P25;P75: 469;824) in the SUPRAtube group ($p<0.001$), equivalent to a mean difference of 213 g (P_{25};P_{75}: 55;569; +50%). The device did not induce adverse events.

Conclusion: Continuous supraglottic aspiration using SUPRAtube is complementary, effective, safe, simple, and inexpensive and reduces the accumulation of oropharyngeal secretions in mechanically ventilated patients. The relevant clinical benefit in terms of preventing and improving tracheobronchitis earlier on was demonstrated by sequential fiberoptic bronchoscopy.

Registration in Clinical Trials: The present study is registered at clinicaltrials.gov NCT03573609.

Keywords: critical care, pneumonia, suction, salivation, intratracheal intubation, mechanical ventilation

Introduction

Aspiration of oropharyngeal contents is the leading risk factor for ventilator-associated pneumonia (VAP). VAP has a high incidence and high mortality.[1] It is reasonable to search for new strategies that complement conventional

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approaches to reduce the risk of bronchial aspiration in these patients. Our hypothesis is that a continuous suction system can help reduce the volume of secretions that accumulate in the oropharyngeal compartment in intubated and mechanically ventilated patients and, in this way, reduce the risk of VAP, its severity, its consequences, and its complications.

Multiple initiatives exist to identify prevention systems for nosocomial pneumonia in the ICU.[2] Since 1994, several studies in the literature have been looking for different measures to reduce the risk of developing ventilator-associated pneumonia due to its impact on the ICU stay, morbidity, and mortality of patients.[3,4] However, none have evaluated the potential usefulness of a supraglottic suction system for preventing ventilator-associated pneumonia.

The first route for lung infection is through microaspiration of microorganisms that colonize oropharyngeal secretions, which can occur in contexts such as a depressed level of consciousness, decreased gag reflex, tracheal intubation, the presence of nasogastric tubes, and stomach stasis, with approximately 45% of healthy individuals aspirating during sleep. Hospitalized patients are commonly colonized by microorganisms acquired from the hospital environment, and up to 75% of seriously ill patients will be colonized within 48h.[5–7] In critically ill patients, mechanical ventilation and nasogastric tube feeding are high-risk factors for aspiration of regurgitated gastric contents.[8] In the ICU setting, although considered protective, endotracheal tubes allow aspiration of oropharyngeal material or bacteria from the gastrointestinal system. Reports of witnessed macroaspirations in critically ill patients range from 1% to 11.7%. Nonetheless, clinically silent, small-volume aspirations are much more common than large-volume aspirations and may occur in up to 94% of patients undergoing invasive mechanical ventilation.[9]

The consequences of aspiration depend on the chemical composition and volume of the aspirated material, as well as the presence or absence of infectious agents, their virulence, and the underlying morbid conditions of the patient, generating pulmonary inflammation, capillary leakage, and oxidative damage. Possible outcomes range from mild pneumonitis to acute respiratory distress and death.[10]

Our group recently completed all phases of conceptualization, functional prototyping, and study of the SUPRAtube device for human use, which has been published and patented.[11] The main objective of the present study was to evaluate the efficacy and safety of the SUPRAtube device in preventing fluid accumulation in the supraglottic region in patients receiving mechanical ventilation through orotracheal tubes. Some of the results of these studies have been previously reported in the form of an abstract.[12]

Methods

Ethics

This study was carried out according to the principles of the Declaration of Helsinki and resolution 8430 of 1993 in Colombia. We obtained approval from the ethics committee of the Cardiovascular Foundation of Colombia ("Fundación Cardiovascular de Colombia", minute reference, 424/2017) on May 30/2017 under the title

> Ensayo Clínico multicéntrico, controlado, aleatorizado para evaluar la eficacia y seguridad del nuevo dispositivo de invención SUPRAtube para prevenir la neumonía asociada a la ventilación mecánica: proyecto SUPRANAV.

Family members provided consent signed by a family member. The study was conducted at two third-level healthcare institutions registered at ClinicalTrials.gov with the identifier NCT03573609.

Support

This study was supported by Ministry of Science and Technology of Colombia (MINCIENCIAS, Colombia), Grant ref. 656677758334, Contract ref. 833-2017; and Research Unit, Fundación Cardiovascular de Colombia (Colombia).

Design, Participants, and Settings

A multicenter, controlled, randomized, parallel clinical trial was conducted with a 1:1 allocation ratio of mechanically ventilated patients. Sample size calculation was done for the secretion volume as primary outcome. The sample size was calculated including an alpha error of 0.05 and a power of 0.8, in a bilateral contrast. Losses to follow-up were estimated at 15%. For an average difference of 200 grams in the aspirate (100 g control group, 300 g intervention

group), with a standard deviation of 340 grams, a total sample of 108 patients was finally obtained including a 1:1 allocation ratio. The inclusion criteria were: adult patients hospitalized in an intensive care unit, intubated and under mechanical ventilation but hemodynamically stable, showing apparent integrity of the upper airways, and basic coagulation tests within the acceptable risk criteria. Excluded patients were who needed orofacial, cervical, or respiratory tract surgical procedures; who were receiving noninvasive mechanical ventilation; who had tracheostomy, shock, uncontrolled local or systemic infection, or severe blood dyscrasia; who had active neoplastic diseases; who had any other physiological alteration or pathology of acute or chronic decompensated disease that was not controlled at the time of selection; or whose family did not consent to participate in the study. The patients' pharmacological history was recorded. The criteria for the comprehensive treatment or the group of complementary examinations that may be required were always in charge of the medical team responsible for the patients and were not modified by participating in any of the phases of the study.

Interventions

Reference Group

Comprehensive standard of care, including preventive strategies, medical therapy, positive pressure MV, and routine procedures for management of oropharyngeal and pulmonary secretions (humidification, patient mobilization, and airway suctioning.

Intervention Group

Comprehensive standard of care plus continuous supraglottic suction with the new SUPRAtube device. The device was positioned in the nadir (decline) oropharyngeal zone for continuous aspiration of supraglottic secretions. The distal end of the device was connected to the vacuum source, and the maximum, minimum, and range pressures reached by the device in operation were verified with a pressure gauge.

For comparisons and evaluation of results, patients in both the control (referent) and study arms received the same set of conventional procedures for cleaning teeth, mouth and pharynx that are applied to all patients under orotracheal intubation and from the first 12 hours of mechanical ventilation. This includes, without exception, tooth brushing every 8 hours, instillation of sterile water in 5–10 mL aliquots in the oropharynx as needed and subsequent suction. Suction is performed using sterile, nontoxic, thermosensitive polyvinyl chloride probes with a diameter of Fr14 and for single use only (Code 1133, Sherleg SAS, 2006; INVIMA health registry 2006 DM-0000097-R1). The probe insertion depth is intended to cover both the mouth and the oropharynx and the supraglottic area. Negative pressure for suction is limited to a maximum value of 80 mmHg. The frequency of instillation and aspiration of sterile water is also protocolized to be performed every 8 hours but can be repeated as necessary depending on the volume of secretions and at the discretion of the transdisciplinary health team. Patients in the SUPRAtube arm received the same care strategies, including dental and oropharyngeal rinsing, instillations and aspirations with the tube, in addition to maintaining the study device with continuous aspiration. In all cases, the volume of saline solution instilled in each of these therapeutic care sessions was strictly recorded.

Random Assignment

To deal with adjudication bias given the unblinded nature of the study, a computer-based randomization sequence was developed and verified by the study coordinators regarding compliance by the research staff from assignment to the end of the study. Opaque envelopes were prepared and sequentially numbered, each containing a card indicating the assignment to the corresponding treatment group. The envelopes were sealed prior to the inclusion of each patient in the study. At the time of assignment, the research staff opened one envelope, without prior knowledge of the assignment, to determine the group to which the patient would be assigned. This method allows to ensure random distribution and prevent any bias in the assignment of patients to the different study arms. The clinical epidemiology staff maintained centralized allocation using the sequential envelopes. Assignment was based on a 1:1 ratio to the usual management group or the SUPRAtube group.

Blinding

The patients were blinded as they were under sedation. Additionally, the data analyst was unaware of the intervention allocation.

Device Operation

SUPRAtube is a sterile and disposable probe inserted through the mouth and nose and placed in the supraglottic space. It has an external cavity with a fenestrated aspiration capsule, which, in its distal portion, is a malleable rhombus attached to a coaxial aspiration tube. Its probe is translucent to visualize the aspirated content, and in its terminal portion, it has a proximal universal connector that allows its connection to a vacuum source (Figure 1). The design and technical details of the invention, including the description of the supraglottic suction element, material, sizes, manufacturer and inventor group along with the validation of its use, are fully described in the pilot study recently published by Ramírez-Sarmiento et al[11] in which aspects of the efficacy and safety of the SUPRAtube device were also evaluated.

Outcomes

The primary endpoint of the study was the volume of aspirated secretions. The total volume of liquid aspirated was expressed as absolute value and as a quotient with respect to the aspiration time; Secondary outcomes were the presence of ventilator-associated events (VAE) defined by the CDC as ventilator-associated conditions, infection-related ventilator-associated complications (IVAC), or possible ventilator-associated pneumonia. These included the group of infectious conditions (such as tracheitis, tracheobronchitis, and pneumonia) and/or noninfectious conditions (such as atelectasis, pulmonary embolism, pulmonary edema, ventilator-induced lung injury, and others) that fulfill the VAE definition. The time frame included 24 hours after extubation. To assess the safety of the use of the device, the possible occurrence of non-serious or serious adverse events was sought and recorded. These included the occurrence of bleeding or lacerations in the oropharynx within 24 hours after extubation; endoscopically visible alterations in the oropharynx (macules, erythema, ulcers, edema, friability, fibrinolysis or necrosis of the epithelium); the appearance of abnormal secretions; the presence of food or bilious coloration of secretions; microbiological changes in aspirated secretions (by direct Gram and KOH stains, as well as aerobic, anaerobic and fungal cultures in aspirated secretions by bronchoscopy); the occurrence of serious adverse events (death, disability and hospital stay); the occurrence of non-serious adverse events

Figure 1 Three-dimensional images showing the three functional components of the SUPRAtube. (**A**) Shows an enlarged view of the elastomeric ellipsoid device which is designed as the intracavitary element inserted through the mouth or nose and advanced to the supraglottis for continuous negative pressure aspiration of secretions; (**B**–**D**) Show the flexible probe and the universal connector for the vacuum pressure source at the other end of the device. Details of the development and fabrication of the device are described in both the body of the manuscript and reference 11 (Ramírez.-Sarmiento A., et al, Med Devices 2021;14:287–297).

(oral ulcers, perforation, bleeding, lacerations, edema and candidiasis); defects in the functions of the device; and total ICU and hospital stays.

Statistical Analysis

The analysis was by intention to treat. The normality of the data was analyzed using the Shapiro–Wilk test. Data following a Gaussian distribution are described as the mean with standard deviation and the intervention groups were compared with Student's *t* test. Non-Gaussian data are presented as medians with 25 and 50th percentiles and were compared using the Mann–Whitney *U*-test. Categorical data were described as n and percentage and, also analyzed using the chi-square test or Fisher's exact. The aspirated volumes and weights were normalized to the unit of time. The presence or absence of macroscopically evident material in trachea and bronchi was analyzed categorically. Median differences are calculated between values of a Y-variable (aspirated volume) for a pair of observations chosen at random from the two study groups, using *cendif* command in STATA-17.

Results

Between July 2018 and March 2021, 893 patients were evaluated in the intensive care units of the participating centers. One hundred eight patients were randomly assigned to the SUPRAtube intervention group (n=54) or the usual management comparison group (n=54). Losses to follow-up represented 5.5% of the included population. The reasons for exclusion and loss to follow-up are listed in Figure 2. Age reached a statistical difference between the two groups [64 (47; 74) vs 57 (39; 68) years, respectively; p=0.0385]. For the other variables, no differences were found between the groups (Table 1).

For the SUPRAtube's secretion aspiration capacity, a more significant collection of secretions was obtained from patients in the intervention group treated with the device, as evidenced by statistically significant differences in total weight and weight subtracted from the instilled volume (net weight) (Table 2 and Figure 3). Additionally, when adjusting for the duration of the device's use a median of 57.6 g of additional secretions was aspirated for each day of device use (p=0.009). Importantly, age did not correlate with neither the volume aspirated nor the weight of the aspiration. No significant differences were observed between the observation time or the instilled volume between the groups, indicating comparability between them.

When comparing the initial and final fiberoptic bronchoscopy findings, a lower proportion of infection-related ventilator-associated complications was found in the SUPRAtube group than in the control group (p=0.007); specifically, tracheobronchitis findings were reduced by nearly 50% when compared to those of fiberoptic bronchoscopy at baseline (RR=0.49; 95% CI=0.30; 0.81). Similarly, it was found that patients receiving the SUPRAtube had significantly more favorable progressions against tracheobronchitis (p=0.003) than did those in the control group, who had 2.5 times greater chances of progressing favorably (RR=2.53; 95% CI=1.25; 5.1). In addition, although there was a trend toward reducing other tissue changes and secretions observed via fiberoptic bronchoscopy, the difference was not statistically significant. Adding up all the abnormal fiberoptic bronchoscopy findings, people assigned to the SUPRAtube group had significantly fewer abnormal fiberoptic bronchoscopy findings postintervention (36% fewer, p=0.007) and 5-fold more favorable progress than did those in the control group (RR= 5.04; 95% CI: 1.22; 20.81). A significantly lower number of KOH-positive patients assigned to the SUPRAtube group was also found (2 patients, 6.25%) than in the control group (7 patients, 25.9%) (p= 0.041). These findings were consistent when the initial culture was compared with the final culture, and a greater proportion of patients with favorable progress regarding KOH results was found in the SUPRAtube group (29 patients, 95.55%) than in the control group (20 patients, 74.1%) (p=0.046). In addition, when evaluating whether any microorganisms were found in the secretion samples, 69.7% positivity for microorganisms was found in the SUPRAtube group in baseline cultures, whereas 42.9% was found in the control group (p=0.035); however, in the final cultures, this significant difference disappeared, indicating that the groups had similar proportions of microbiological findings in the cultures. No significant differences were observed regarding favorable changes for any microorganism (p=0.375).

No significant differences were found between the comparison groups regarding ICU stay, hospitalization days before mechanical ventilation, days of mechanical ventilation, or discharge status (Table 3).

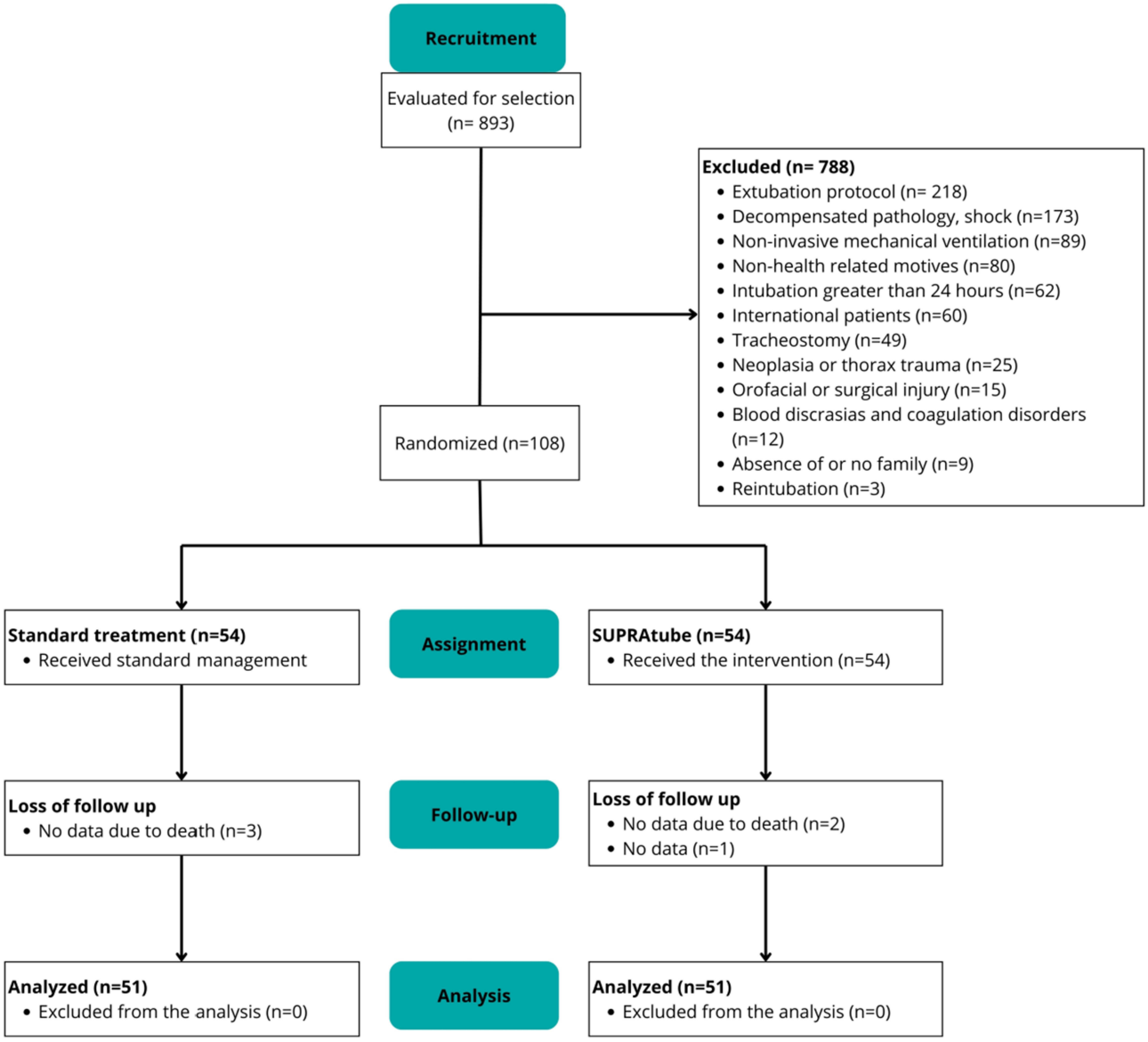

Figure 2 Study Flow Diagram.

Regarding device function and safety, occlusion associated with traces of blood or very thick secretions was observed in 15.7% of patients, device displacement in 17.6%, and a combination of the two in 11.7%. Suspicion or evidence of spontaneous recoil requiring verification and repositioning under laryngoscopic visualization was 3% of cases. There were no serious adverse events. Figure 4 includes photographs as an example of the video bronchoscopic view of the SUPRAtube device and its relationships with some of the anatomical structures of the supraglottis. Purulent secretions in the nose (7%), minor epistaxis (12%), blood traces in the pharyngeal-supraglottic aspirate apparently coming from the nasopharyngeal sphere (2%) or tracheo-bronchial sphere (8%) were identified. There were no ulcers or lacerations justifying bleeding. Edema was often observed in supraglottis (15%), mainly in the initial endoscopic evaluations, and suspected oral candidiasis was present in one patient (Table 4).

Table 1 Baseline Characteristics of the Participants

Characteristics	Categories, Central Tendency, Dispersion of Values	Control	SUPRATUBE	Total
		n=51	n=51	n=102
Age, years	Median (min; max) Under 40 years 40 to 59 years 60 or older	64 (23; 83) 5 (9.8) 15 (29.4) 31 (60.8)	57 (19; 85) 13 (25.5) 15 (29.4) 23 (45.1)	62.5 (19; 85) 18 (17.7) 30 (29.4) 54 (52.9)
Sex, n (%)	Male	27 (52.9)	35 (68.6)	62 (60.8)
Body mass index, kg/m^2	Median (min, max)	26 (16.6, 41.5)	24.7 (14.7, 51.1)	257.4 (14.7, 51.1)
Institution, n (%)	HIC ICV	46 (90.2) 5 (9.8)	40 (78.4) 11 (21.6)	86 (84.3) 16 (15.7)
Comorbidity, n (%)	Yes	24 (47.1)	30 (58.8)	54 (52.9)
Pharmacological history, n (%)	Yes No No data	25 (49) 19 (36.5) 7 (13.7)	17 (33) 29 (58) 4 (7.8)	42 (41.2) 48 (47.1) 12 (10.8)
With previous antimicrobial treatment, n (%)	Yes	36 (70.6)	32 (62.8)	68 (66.7)
With current antimicrobial treatment, n (%)	Yes	47 (92.2)	44 (86.3)	91 (89.2)
Days prior to the study on MV, median (min; max)		1 (0;4)	1 (0; 5)	1 (0; 5)
Tube Gauge, n (%)	7 or less 7.5 8 8.5	7 (13.7) 25 (49) 19 (37.3) 0	2 (3.9) 29 (56.9) 17 (33.3) 3 (5.9)	9 (8.8) 54 (52.9) 36 (35.3) 3 (2.9)
Ventilatory mode, n (%)	AC/VC plus AC/CP AC/CV Bilevel	7 (13.7) 14 (27.5) 30 (58.8) 0	15 (30) 14 (28) 20 (39.2) 2 (3.9)	22 (21.8) 28 (27.7) 50 (49) 2 (2)
Ventilatory parameters	Tidal volume, median (min; max) Minute ventilation, median (min; max) $Fi0_2$, median (min; max) PEEP, median (min; max)	390 (320; 610) 7.1 (3.8; 12) 0.45 (0.3; 1) 7 (6; 14)	423 (230; 697) 7.5 (4.2; 14) 0.40 (0.3; 1) 7 (6; 14.5)	400 (230; 697) 7.3 (3.8; 14) 0.45 (0.3; 1) 7 (6; 14.5)
Vital signs	Heart rate, mean (SD) Respiratory rate, median (min; max) Systolic blood pressure, mean (SD) Diastolic Blood Pressure, mean (SD) Mean Blood Pressure, median (min; max) Temperature, mean (SD) Oximetry, median (min; max)	85.6 (22) 10 (10; 20) 127 (25.8) 64.4 (14.5) 82.7 (59; 145.3) 36.2 (0.8) 97 (83; 100)	88 (24) 11 (10; 24) 129.4 (22) 67.8 (12.5) 85 (68; 117) 36.4 (0.9) 96 (35; 100)	87 (23) 12 (10; 24) 128.2 (23) 66, 1 (13.6) 84.7 (59; 145.3) 36.3 (0.9) 97 (35; 100)

Note: Initial descriptive demographic, anthropometric and general clinical characteristics of the patients included in the study. Results expressed as the mean and standard deviation (SE), median (minimum-maximum), n (%) or median and interquartile range.

Abbreviations: HIC, Hospital Internacional de Colombia; ICV, Instituto Cardiovascular-Fundación Cardiovascular de Colombia; MV, mechanical ventilation; ICU, intensive care unit.

Discussion

Most recent research on suction strategies for preventing ventilator-associated complications has focused on removing secretions accumulated at the subglottic level and above the cuff of the endotracheal tube.[13–15] Currently, the most widely used system for suctioning secretions in the clinical environment is intermittent suction probes, which require handling by health professionals and can eventually cause morbidity (pain, lacerations, bleeding). Based on experience in the clinical arena, we believe that this practice can be improved, which justifies the fact that we recently designed and

Table 2 Aspirated Supraglottic Fluid According to the Study Groups

Characteristics	Control n=51	SUPRAtube n=51	Difference	Total	p-value
	median (min; max)	median (min; max)	median (min; max)	median (min; max)	
Observation time, hours	84 (12; 359)	96 (7; 456)	12 (30.2; 54.3)	85 (7; 456)	0.9199
Instilled Volume during the study, mL	190 (10; 545)	210 (10; 670)	60 (60.3; 100.3)	195 (10; 670)	0.2131
Total weight collected during the study, gr	623 (399; 1247)	847 (379; 1779)	224 (39.5; 408.5)	704 (379; 1779)	0.0002
Net aspirated weight during the study, gr	415 (144; 997)	624 (389; 1339)	209 (118.1; 299.9)	477 (144; 1339)	<0.001
Weight in g/day	131 (30.1; 812)	193.8 (24.9; 1361.1)	62.8 (7.5; 118.1)	162.7 (24.9; 1361.1)	0.009

Note: Descriptive variables of the follow-up time for the evaluation effects of supraglottic aspiration with the conventional method and with the SUPRATUBE device in the two study groups.

patented an innovative device for continuous supraglottic aspiration, which could be evaluated in a pilot study in humans and has allowed us to advance to the present trial of clinical trial types in ICU patients who were intubated and mechanically ventilated.[9] The potential clinical benefits that have justified both the design and evaluation in terms of safety and efficacy of the SUPRAtube device translate into its ability to reduce the volume of fluid that accumulates in the oropharynx in mechanically ventilated patients. The plausible argument to consider that this effect is beneficial has to do with the lower the supraglottis content, the lower the risk of intermittent or continuous bronchoaspirations. Consequently, the risk of infectious and non-infectious complications associated with these events could be lower. In this line, our study supports that continuous supraglottic suction using a SUPRAtube can reduce the volume of secretions that accumulate in the oropharynx of intubated and mechanically ventilated patients. The results of the present study are discussed in terms of six main concepts:

First, it is important to highlight what an endotracheal tube represents. The use of an endotracheal tube is unavoidable when necessary to ensure entry of air, and a pneumo-tamponade device is used to partially fixate the tube and prevent air leakage and entry of materials from the supraglottis into the trachea and lung. However, it is not 100% airtight, not entirely innocuous, or even a reservoir factor where bacteria can settle and form a biofilm with great infectious capacity.

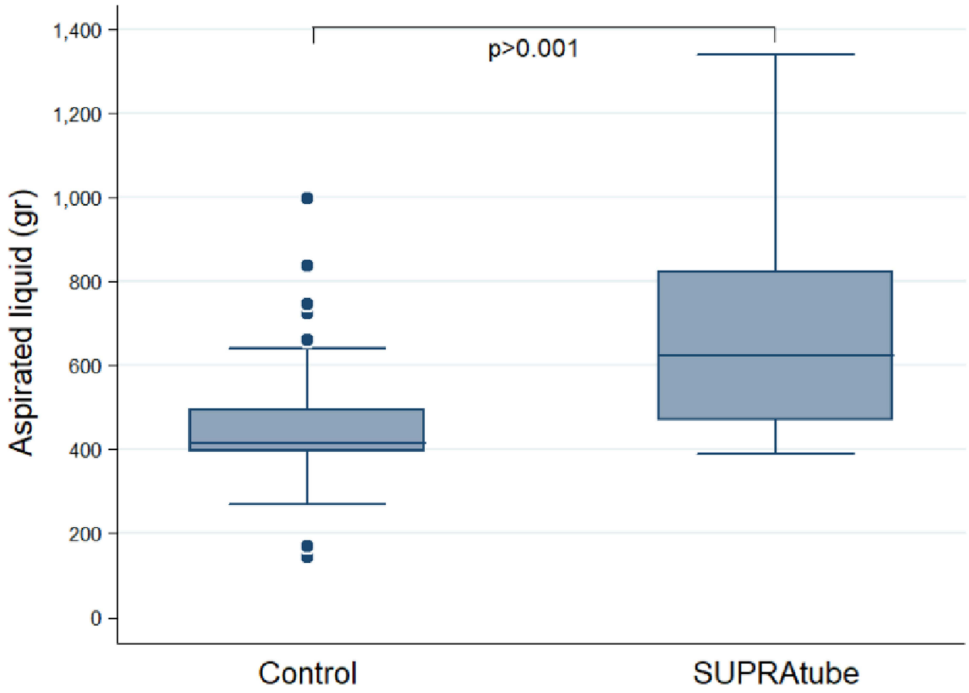

Figure 3 Efficacy of continuous supraglottic suction with the SUPRAtube device in mechanically ventilated patients. Results are expressed in terms of the net weight of total aspirated fluid (y-axis) in the two study groups, the control arm and the SUPRAtube group (x-axis). For a review of the normalized values per unit of time, refer to Table 2.

Table 3 Hospital Outcomes According to the Intervention Group

Outcome	Control	SUPRATUBE	Total	p-value
	n=51	n=51	n=102	
Days in ICU, median (min; max)	3 (1; 51)	5 (2; 71)	4 (1; 71)	0.7099
Days in hospital, median (min; max)	3 (1; 129)	6 (2; 125)	4 (1; 129)	0.6536
Days prior to MV, median (min; max)	0 (0; 4)	0 (0; 5)	0 (0; 5)	0.9294
Days of MV, median (min; max)	2 (1; 32)	2 (1; 72)	2 (1; 72)	0.26
Discharge status, n (%)				
Discharge	22 (43.14)	25 (49.02)	47 (46.08)	
Death	25 (49.02)	17 (33.33)	42 (41.18)	
Remission	4 (7.84)	9 (17.65)	13 (12.75)	0.173

Note: Values of the duration of hospital care before mechanical ventilation, duration of this, and situation of patient discharge.
Abbreviation: MV, mechanical ventilation.

Endotracheal tubes with a tracheal suction port (subglottic) exist. Several controlled trials have evaluated[16,17] the use of such modified endotracheal tubes that allow continuous aspiration of subglottic secretions versus traditional endotracheal tubes; the results showed that subglottic aspiration can reduce the incidence of VAP including late-onset VAP.[17] Gopal et al showed that the Venner-PneuX® VAP prevention system is associated with a significant reduction in VAP, and potentially lead to significant cost reductions, The authors suggested it should be implemented as part of the VAP reduction bundle.[16] Diffusion in the usual clinic has been limited by their high cost and the frequency of dysfunction (occlusion), which prevents them from being maintained by continuous aspiration.Several other authors have evaluated subglottic suctioning (above the cuff of the endotracheal tube, SACETT) and compared it with that of the standard endotracheal tube (SETT) in postoperative neurological patients. The strategy decreased the incidence of respiratory infection and the use of antibiotics; there were no statistical differences between the groups. Still, there was a decrease in the incidence of pneumonia, days of stay in the ICU, or mortality rate. Fujimoto et al[18] aimed to compare the efficacy of continuous and intermittent subglottic secretion drainage (SSD) in preventing VAP on adult postoperative patients who were expected to undergo mechanical ventilation for more than 48 hours. Although continuous SSD did not reduce the incidence of VAP, it reduced the length of mechanical ventilation and ICU stay when compared to intermittent SSD.

Second, we must highlight that continuous suctioning of oral secretions in intubated and mechanically ventilated patients has been evaluated in several previous investigations. In general, it has been shown that the incidence of VAP does not decrease. Nonetheless, a clinical benefit is obtained in terms of shorter mechanical ventilation time (99.5 ±

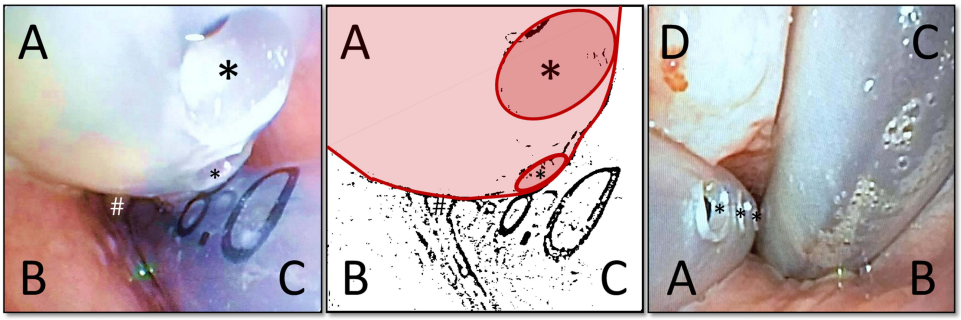

Figure 4 Images obtained during videoendoscopic evaluations of two of the patients in whom the SUPRAtube device was inserted and put into operation. (**A**) Ellipsoid elastomeric component of the SUPRAtube as seen endoscopically when placed in the supraglottic area of intubated patients; in the contour-drawn rendered figure, the elastomeric component is highlighted as the red shaded area; (**B** and **C**) contact of the ellipsoid elastomeric component of the SUPRAtube with the postero-lateral wall of the supraglottis; (**C**) orotracheal tube for mechanical ventilation; (**D**) anterior wall of the supraglottis; (*): visible foramina of the suction elastomeric component; (#): left vocal cord.

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Table 4 Functional and Safety Findings of the Device

Findings of Defects in Function	n (%)
No defect	28 (54.90)
Occlusion	8 (15.69)
Displacement	9 (17.65)
Occlusion and displacement	6 (11.76)
Adverse events due to the device	
Without adverse events	47 (92.2)
With some adverse event	4 (7.8)
Serious Adverse Events	
Death	0
Disability/invalidity	0
Prolongation of hospital stay	0
Non-serious Adverse Events	
Oral mucosal ulcer	0
Oropharyngeal perforation	0
Cheilitis	0
Oropharyngeal bleeding	2 (3.92)
Edema	1 (1.96)
Candidiasis	1 (1.96)
Excoriations	0
Lacerations	0

Note: General descriptive variables were included in the evaluation of the operation and safety of the device throughout the study period.

47.1 h vs 159.9 ± 94.5 h) and fewer days of ICU stay (6.3±2.1 vs 9.8±4.8 days) in patients who underwent intermittent aspiration.[11] In this sense, we did not find that the SUPRAtube was significantly associated with the duration of mechanical ventilation or the duration of stay in the ICU between the two study groups. It is possible that there are subgroups of patients more likely to benefit from continuous aspiration or that some patients with worse outcomes have remained in the SUPRAtube group despite randomization.

Third, the present study shows that SUPRAtube device effectively aspirated the oropharyngeal content that accumulated both by extrinsic instillation and intrinsic production. These results, expressed in terms of the volume and weight of normalized oropharyngeal secretions per unit of time, confirm, among others, that this clinical risk factor has been underestimated in the clinical setting, specifically in terms of the volume-weight of the aspirated liquid. This striking demonstration of the significant differences in the volume and weight of fluid aspirated by continuous aspiration via the SUPRAtube vs conventional intermittent aspiration allows us to continue attempting to develop suction catheters that reduce the volume of oropharyngeal secretions as a strategy to prevent VAP in ICU patients. In the reviewed literature, no studies have compared the suction capacity of secretions suctioned by suction devices.[19]

Fourth, the operation of the SUPRAtube device has been limited to operating under controlled, low, negative pressure. The research team has empirically defined the limit, which is equal to −30 mmHg. We have shown that, in the conventional clinical environment, suction pressures change frequently (albeit in intermittent and short periods) in and due to uncontrolled conditions in routine clinical practice (mechanical defects, patient status, respiratory therapy protocol). Despite this, transient pressures incidentally detected with values greater than −100 mmHg with the use of the device did not generate any direct local adverse events in the respiratory epithelia of the patients as assessed by respiratory endoscopy.

Fifth, it is essential to highlight that 100% of the patients studied showed an accumulation of liquid in the oropharyngeal and supraglottic spheres. The aspirated volume ranged between 399 and 1779 mL, equivalent to a total weight of 25–1361 g during the study period. The foam and density of the liquid account for the differences between the volume and weight. The SUPRAtube group had markedly greater amounts of aspirated fluid (151% greater, $p<0.001$) than did the reference treatment group, both in absolute terms and normalized per unit of time.

Sixth, we must highlight that the new SUPRAtube device represents a complementary, nonredundant, effective, and safe method for aspirating the supraglottic cavity in patients who are receiving orotracheal intubation and mechanical ventilation. The added value of using the SUPRAtube compared to the usual intermittent suction strategy is represented by two fundamental aspects: greater suction capacity of the liquid content that accumulates in the supraglottic and oropharyngeal spheres of these patients and a relevant clinical benefit in terms of preventing and improving tracheobronchitis earlier on, as evaluated by sequential fiberoptic bronchoscopy. The SUPRAtube is an inert device, not an antiseptic or antibiotic strategy, so it does not impose biological selection pressure on conflicting germs. Continuous supraglottic aspiration using the SUPRAtube implies, by definition, that the device is inserted through the mouth or nose and represents an additional foreign body to the nasogastric tube and the endotracheal tube itself. Nevertheless, there was no evidence of traumatic or local infectious macroscopic alterations with the device, which indicates its safety.

This study has limitations that must be mentioned. Due to the intrinsic nature of the clinical trial design, one limitation is the difficulty of randomizing patients according to the risk of vomiting, macroregurgitation, sinus secretions, or more significant oropharyngeal secretions. We cannot define the clinical impact of intermittent suction modalities using the same device. We have not evaluated the possibility of using the SUPRAtube in pediatric patients. There are no data on the safety of operating the device for extended periods. No information exists regarding the potential complementary benefits of intermittent instillation of antiseptic solutions through the SUPRAtube to reduce risks related to bacterial biofilms and reduce oropharyngeal inoculum. Finally, although we promote its insertion through the mouth, we must consider the possible alternative of nasal introduction. The study was not powered to address secondary outcomes such as ventilator-associated events or microbiological cultures; further trials will be needed to assess those outcomes. It seems reasonably justified to evaluate the impact of SUPRAtube on hard clinical outcomes such as morbidity associated with ventilation, direct and indirect costs, as well as mortality of patients candidates for its use. It is especially important to suggest that the SUPRAtube device should be evaluated in clinical trials to determine its safety and clinical efficacy in preventing VAP.

Conclusion

Continuous supraglottic aspiration using the SUPRAtube device is a relevant, justified, feasible, simple, effective and safe additional therapeutic strategy for preventing the accumulation of oropharyngeal secretions in intubated and mechanically ventilated patients. Reducing the inoculum by bronchial aspiration may reduce the incidence and severity of complications such as tracheobronchitis and nosocomial pneumonia associated with mechanical ventilation.

Data Sharing Statement

The authors intend to share deidentified participant data, including demographic and clinical characteristics and specific data regarding the device's safety and efficacy, with other individuals. The data are available upon request from the corresponding author (mauricioorozco@fcv.org).

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Disclosure

Dr Mauricio Orozco-Levi reports a patent SUPRAtube. This device has received a patent as a utility model licensed to (ref. NC2016/0002059 Resolution 466). Dr Alba Ramírez-Sarmiento reports a patent NC2016/0002059 Dispositivo médico de aspiración supraglótica en pacientes ventilados mecánicamente licensed to Resolution 466 of the Superintendence of Industry and Commerce, Colombia. The authors report no other conflicts of interest in this work. An abstract of this paper was presented at the ERS Congress 2019 (Madrid, Spain) - Late Breaking Abstract conference

talk, with interim findings. The abstract was published in the European Respiratory Journal 2019, with DOI https://doi.org/10.1183/13993003.congress-2019.RCT5098.

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