ORIGINAL ARTICLE

Sleep Science

Continuous Positive Airway Pressure: Is it a route for infection in those with Obstructive Sleep Apnoea?

Liam Mercieca [1]*
Richard Pullicino [1]
Kyra Camilleri [1]
Rodianne Abela [2]
Sean Apap Mangion [1]
Julian Cassar [1]
Matthew Zammit [1]
Christine Gatt [2]
Christopher Deguara [3]
Christopher Barbara [2]
Peter Fsadni [1]
Stephen Montefort [1]

[1] Department of Medicine, Mater Dei Hospital, Msida, Malta.
[2] Bacteriology Laboratory, Pathology Department, Mater Dei Hospital, Msida, Malta.
[3] Sleep Laboratory, Department of Medicine, Mater Dei Hospital, Msida, Malta.

Corresponding author: Liam Mercieca, Sleep Laboratory, Department of Medicine, Mater Dei Hospital, Dun Karm Street, Msida, MSD2090, Malta.
E-mail: liam.mercieca@gov.mt
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ABSTRACT

Introduction: Continuous positive airway pressure (CPAP) is the standard treatment for obstructive sleep apnoea (OSA), with limited data about the prevalence of respiratory infections and microbial colonization in these patients. **Objectives:** The aim of this study was to determine if CPAP use is associated with respiratory infections and to identify the organisms that colonize or infect these patients. **Method:** A retrospective, case-controlled study in patients diagnosed with OSA was carried out. 137 patients were recruited and interviewed using a questionnaire. A nasal swab was taken from each patient. Patients using CPAP machines had swabs taken from masks and humidifiers. **Results:** 66 (48.2%) patients received CPAP treatment with 60.6% of them having a heated humidifier. 78.8% were male, with the majority using a full face mask (63.6%). No significant difference was seen in the prevalence of rhinosinusitis, lower respiratory tract infections and hospital admissions for pneumonia between CPAP and non-CPAP treated patients. The presence of a humidifier did not influence the prevalence of infections. Commensal flora was predominantly cultured from nasal swabs from both patient groups. Coagulase Negative Staphylococci and Diphtheroids were the main organisms cultured from masks and humidifiers respectively. **Conclusions:** This study shows that the use of CPAP, choice of mask and humidifier have no significant impact on the prevalence of infections and micro-organisms isolated. This is very reassuring to the physician prescribing CPAP therapy and users.

Keywords: Respiratory tract infections; Obstructive sleep apnea; Continuous positive airway pressure; Drug-related side effects and adverse reactions.

INTRODUCTION

Background & Pre- Specified Hypothesis

Continuous positive airway pressure (CPAP) is the treatment of choice for Obstructive Sleep Apnoea (OSA), demonstrating elimination of apnoea whilst also improving OSA's neurocognitive and cardiovascular sequelae[1].

Compliance to CPAP treatment was negatively impacted by reported side effects during CPAP treatment[2], the principal complaint being upper airway dryness. Whilst this was alleviated through the introduction of humidifiers attached to CPAP machines[3], research has established that humidifiers may harbour multiple bacterial colonies, some of which are pathological in nature[4].

The hypothesis explored (summarised in Figure 1) implies that airway dryness due to CPAP leads to impairment of mucosal barrier and predisposes to upper and lower respiratory tract infections.

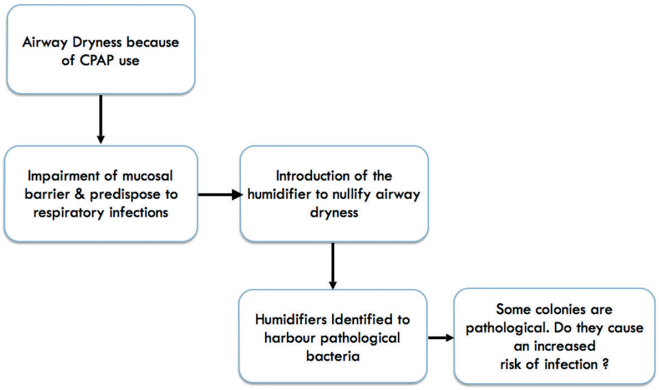

Figure 1. Continuous positive airway pressure (CPAP) infection hypothesis.

However even with the introduction of humidifiers (effectively nullifying airway dryness), pathological bacterial colonisation in such devices may be transmitted to CPAP utilising patients to airway infections.

It is imperative that increased infection rates are identified; with many OSA patients being already susceptible to infection; including diabetics, smokers and those with narrow & congested airway. Furthermore, infection resulting from CPAP use may further exacerbate patients' co-morbidities such as those with chronic congestive heart failure and asthma.

The study was devised to explore this hypothesis**,** with data being scarce on the correlation of infections with non-invasive mechanical ventilation[5,6].

OBJECTIVES

The primary aim of this study was to determine whether use of CPAP machines (humidified & non-humidified) is associated with increased rates of respiratory tract infections and hospitalisation.

The secondary aim was to compare bacterial flora of CPAP and non-CPAP utilising OSA patients.

Other sub-analysis to identify differences in bacterial flora between the nasal and full facemask users and use and cleaning patterns of apparatus were also carried out.

METHODS

Study Design

A retrospective, case-controlled study was carried out from October 2013 to May 2014, once ethical approval was granted.

Subjects were recruited from the local sleep clinic. The inclusion criteria were patients who were diagnosed with OSA according to polysomnography (Apnoea-Hypopnea Index (AHI) or Respiratory Distress Index ≥15 episodes/hour) and no other underlying sleep, medical, or neurological conditions, or drugs that could explain their underlying sleep breathing disorder[7].

Patients were divided into a study group including those who were treated with CPAP and a control group of newly diagnosed OSA patients who were still not using CPAP. These were matched according to age and gender.

After obtaining informed consent, participants were asked to fill in a questionnaire. This considered co-morbidities, smoking history, vaccinations, symptoms and treatment of respiratory tract infections in patients as well as level of CPAP use and hygiene maintained.

A swab was taken from the nasal passages of all patients and from masks and humidifiers in those using CPAP. Swabbing was carried out according to a pre-specified standard operating procedure. Culture analysis was carried out on the swabs according to a specified protocol using charcoal swabs. Swabs were inoculated on tryptone soya agar plates and incubated at 28-30°C in air for 24-48hrs. The organisms cultured were identified down to genus or species level using Gram stain, appropriate biochemical tests and automated identification system (VITEK® 2 Compact, Biomérieux) as per local laboratory standard operating procedures.

All the aforementioned data was anonymized, inputted and processed into a database according to the local Data Protection act. Statistical analysis was carried out using Statistical Package for Social Sciences (SPSS©) version 20. Fisher's exact test and Chi-squared test for association were used for comparison studies.

Study Size

There are no epidemiological studies concerning the prevalence of OSA in Malta, therefore the prevalence rate in Europe (5 to 7%) was used[8]. The optimal sample size at a power calculation of α=80%, accounting for design effect and non-response or recording error was determined to be 120 participants.

RESULTS

A total of 137 (n=108) patients were recruited in the study (see Figure 2). The mean patient age was 53.83 years.

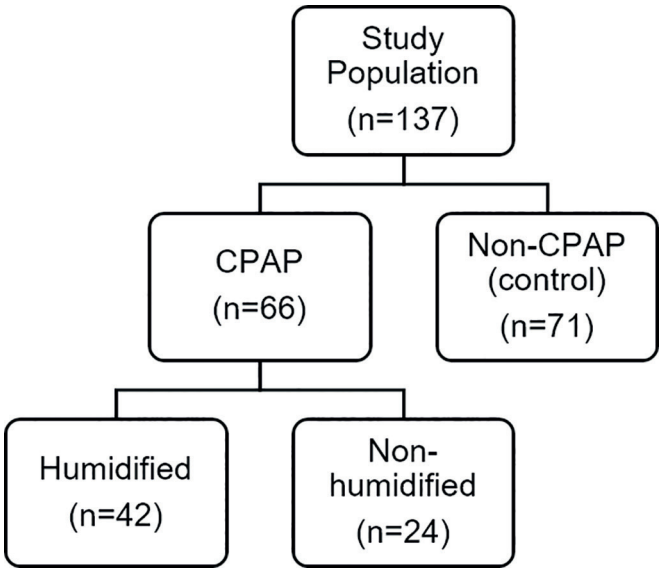

Figure 2. Study population subgroups and sizes. CPAP=continuous positive airway pressure.

66 patients were assigned to the study group (on CPAP) with a median AHI score of 33.9 (mean=36.03), a median Oxygen Desaturation Index (ODI) score of 27.10 (mean=24.94) and a median BMI score of 36.83kg/m^2 (mean=37.56kg/m^2).

71 patients were assigned to the control group (not on CPAP) with a median AHI score of 38.71 (mean=38.23), a median ODI score of 29.00 (mean=33.88) and a median BMI score of 36.11kg/m^2 (mean=37.68kg/m^2).

The commonest comorbidities included hypertension (55%), diabetes mellitus (31%), hyperlipidaemia (19%), asthma (15%) and ischaemic heart disease (14%).

20% (*n*=28) of the study population were smokers with a mean pack-year of 44.75 (*SD*=35.20) and 38.69% (*n*=53) were ex-smokers. 36.50% (*n*=50) took the influenza vaccine in the previous year and 2.19% (*n*=3) took the pneumococcal vaccine over the past 5 years.

Comparison of infection rates between CPAP and non-CPAP patients

There was no significant difference reported in lower respiratory tract symptoms (cough, fever and coloured sputum production) over the past year between CPAP (*n*=14) and non-CPAP (*n*=11) patients (*p*= .527).

Acute rhinosinusitis (bacterial and viral) was defined according to validated criteria set by Rosenfeld et al.[9].

Table 1 demonstrates that there was no statistical difference in acute rhinosinusitis rates between CPAP and non-CPAP patients. Furthermore there was no difference between the humidified (*n*=8) and non-humidified (*n*=7) groups (*p*= .548).

There was no difference in antibiotic treated chest infections between CPAP (*n*=15) and non-CPAP (*n*=11) patients (*p*= .392). Also there was no difference in hospitalization rates for pneumonia between the two groups (CPAP, *n*=7) (non-CPAP, *n*=2) (*p*= .097).

Table 1. Bacterial and Viral Rhinosinusitis in CPAP and non- CPAP groups. CPAP=Continuous positive airway pressure.

	CPAP (n=66)	Non-CPAP (n=71)	p value (Fisher's exact test)
Bacterial and Viral	16	11	0.393
Bacterial	5	6	0.745
Viral	11	5	0.119

Comparison of the clinically relevant and commonest organisms cultured in nasal swabs between CPAP and non-CPAP patients

There was no statistical difference in type and frequency of organism cultured as shown in Table 2.

Table 2. Nasal swab cultures between CPAP and non-CPAP patients. CPAP=Continuous positive airway pressure.

	CPAP (n=66)	Non-CPAP (n=71)	p value (Fisher's exact test)
E.coli	1	0	0.496
MRSA	10	14	0.493
Coagulase negative staphylococci	47	50	0.631
Diphtheroids	33	29	0.461
Bacillus	10	14	0.502
Staphylococcus aureus	9	8	0.802

Comparison of the clinically relevant organisms cultured in CPAP patients between nasal mask and full face mask users

There was no statistical difference in organisms cultured between CPAP patients using nasal mask and full facemask as shown in Table 3.

Table 3. Clinically significant organisms cultured between different mask users.

	Nasal mask	Full Facemask	p value (Fisher's exact test)
E. coli	0	0	-
MRSA	0	1	1
Coagulase negative staphylococci	9	18	0.587
Diphtheroids	2	3	1

Use & Cleaning of Apparatus

Full facemasks were used by 62.12% (*n*=41) of this patient group while the rest (n=25) used nasal masks. 63.68% (*n*=42) were using a humidifier. The mean duration between change of mask was 11.48 months (*SD*=10).

The majority of patients (89.39%, *n*=59) reported to using CPAP on a daily basis with an average duration of 6.32 hours per day (*SD*=2.03). Cleaning patterns of the apparatus are shown in Table 4.

The mean number of times the water of the humidifier was changed was 6.21 times per week (*SD*=1.71).

A number of guidelines[10,11] were consulted and a standardised cleaning procedure devised to be used as a standard for comparison of collected data (Table 5).

Table 4. Frequency of cleaning of CPAP apparatus. CPAP=Continuous positive airway pressure.

Apparatus	Do you ever clean your apparatus?		Number of times cleaned per week (mean)
	No	Yes	
Mask	37.88% (n=25)	62.12% (n=41)	4.5 (SD=0.43)
Tubing	83.34% (n=55)	16.67% (n=11)	2.27 (SD=2.41)
Non-Disposable Filter	80.30% (n=53)	19.70% (n=13)	2.36 (SD=2.17)
Humidified Reservoir (if present)	47.62% (n=20)	52.38% (n=22)	3.44 (SD=2.86)

Table 5. Cleaning of Apparatus Guidelines.

Equipment	Cleaning Frequency	Instructions	Disinfecting Frequency
Non-Disposable Filters	Weekly	(1) Mild soapy water (2) Rinse & Air dry	Not required
Tubing	Daily	(1) Mild soapy water (2) Rinse & air dry	Once a week
Mask/ Nasal Pillows	Daily	(1) Mild non-lotion detergent & rinse with warm soapy water (2) Air Dry	Once a week
Humidifier reservoir	Daily	(1) Empty remaining water after each use. Immerse humidifier in warm soapy water (2) Rinse & air dry	Once a week

DISCUSSION

Contrary to the proposed hypothesis, the study exhibits no significant difference between the CPAP and non-CPAP (nasal and full mask) groups in terms of infection rates and comparisons between commonest & clinically relevant organisms. Full detailed list of organisms cultured can be found in Appendix A (Table A1).

With non-invasive ventilation exhibiting a clear improvement in cardiovascular mortality and morbidity in OSA patients[12-14], it is of immense reassurance that CPAP machines do not contribute to increase respiratory tract infections in OSA patients.

Furthermore, patients utilising a humidifier did not have increased rates of acute rhinosinusitis when compared to those without, thus enabling safe use whilst enhancing patient compliance. The study population displayed good compliance levels; the majority (89.39%) reported using CPAP on a daily basis with an average duration of 6.32 hours. Reasons for non-compliance were mainly discomfort with the machine and airway dryness. Such scenarios can be tackled through use of a humidifier adjunct.

On comparison, poor cleaning of apparatus is exhibited in our study population (Table 4), especially when considering that none of the CPAP apparatus was cleaned on a daily basis.

Despite poor sanitation & cleaning patterns, the negligible association with increasing respiratory tract infection rates further re-affirms the safety of CPAP and humidifier use.

The questionable concern with regards transfer of infection from CPAP apparatus was answered by very few studies, showing conflicting results. Sanner et al.[5] suggested that patients using CPAP therapy were at an increased risk of upper airway infections compared to non-CPAP patients. Contrary, Chin et al.[6] demonstrated that a positive culture in the CPAP reservoir does not have any clinical impact.

This study supports the results obtained by Chin et al.[6] It included a questionnaire assessing for acute rhinosinusitis (viral and bacterial), lower respiratory tract infections and swabbing of the mask and humidifier. Furthermore nasal swabs were taken and compared with equipment colonisation and infection rates. This study shows that despite using CPAP there are no differences in bacterial nasal colonisation rates and types between CPAP and non-CPAP users.

This demonstrates that a positive culture in the CPAP reservoir does not have any clinical impact and does not lead to increased respiratory tract infections. Our results contradict those obtained by Sanner et al.[5] possibly because they did not have an adequate control group as suggested by the authors themselves. Moreover Chin et al.[6] and this study included bacterial cultures.

Due to the study's design, the researchers were not blinded to the patient's status, which could have led to an element of ascertainment bias. Recall and response bias could also be present in the questionnaire answers. Although it was beyond the aim of this study, a third control arm consisting of non-OSA patients might have helped to elucidate differences in infection rates and nasal colonization, if present. The retrospective design of our study is another limitation since it prevents preview randomisation of the groups. Matching for age and gender was done but other confounding factors could have been present. Our study indicates that CPAP use in OSA patients does not increase respiratory tract infection rates but further research through a randomised prospective study is needed.

CONCLUSIONS

The study clearly demonstrates that CPAP use in OSA patients does not increase upper and lower respiratory tract

infections. It also illustrates that there is no difference in the nasal flora between OSA patients with or without CPAP treatment.

This is reassuring to the physician prescribing CPAP therapy and to the patient himself as infective risk is not increased with CPAP & humidifier use. The study promotes increased use of humidifiers, reducing on- compliant symptoms of dry mouth. Companies producing these CPAP machines should also note these results but should not desist in recommending regular cleaning of mask, tubing and humidifier together with filter change on a regular basis to patients utilising their machines.

OTHER INFORMATION

Ethics

The study received approval from the University of Malta Research Ethics committee.

Funding/Conflicts of Interest

None declared.

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