

## Brief report

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# Nebulized medication is not associated with nosocomial infections. A pilot study

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## ABSTRACT

**Introduction.** Nebulized devices are commonly used in the treatment of respiratory infection, and other respiratory diseases. It has been reported nosocomial infections in cystic fibrosis patients as a result of the use of contaminated devices. However, little is known about nosocomial infections secondary to aerosolized therapy in COPD patients admitted for acute exacerbation.

**Methods.** Thirty consecutive patients (13 males) were included. All of them received aerosolized medication. Each patient used their own facemask and nebulizer cup, which were stored in the room after its use. Samples from nebulizer cups were obtained on days 0, 4 and 7. In addition, sputum samples were obtained on day 0 (prior to any nebulization) and on day 7, and cultivated in enriched media.

**Results.** Only nine nebulizer cups had positive microbiological cultures. Coagulase negative staphylococci (CoNS) were isolated in all cases. Sputum samples could be obtained in 27 patients. None grew CoNS after 7 days of aerosolized therapy. Gram-negative non-fermenting bacilli were isolated in three patients without concomitant grown in nebulizer cups.

**Conclusions.** We did not find any nosocomial infection related to aerosolize medications in COPD patients admitted for acute exacerbation.

## El empleo de nebulizaciones no se asocia con infecciones respiratorias nosocomiales. Un estudio piloto

## RESUMEN

**Introducción.** Los dispositivos para nebulizaciones se emplean frecuentemente en el tratamiento de las infecciones, y otras patologías respiratorias. Existen comunicaciones sobre infecciones nosocomiales en pacientes con fibrosis quística como resultado de la utilización de dispositivos contaminados. Sin embargo, poco se sabe acerca de las infecciones nosocomiales secundarias a la terapia en aerosol en pacientes con EPOC ingresados por exacerbación aguda.

**Métodos.** Treinta pacientes consecutivos (13 varones) fueron incluidos. Todos ellos recibieron la medicación en forma de aerosol. Cada paciente utilizó su propia máscara y cazoletas de nebulización, que se dejaron en la habitación después de su uso. Las muestras de las cazoletas de nebulización se obtuvieron en los días 0, 4 y 7. Además, se obtuvieron muestras de esputo en el día 0 (antes de cualquier nebulización) y en el día 7, cultivándose en medio enriquecido.

**Resultados.** Sólo nueve cazoletas de nebulización tuvieron algún cultivo positivo, siendo estafilococos coagulasa negativos (ECN) en todos los casos. Se obtuvieron muestras de esputo en 27 pacientes. En ningún caso se obtuvo crecimiento de ECN tras 7 días de tratamiento con aerosolterapia. Finalmente en tres pacientes se obtuvo crecimiento de un bacilo gramnegativo no fermentador en el esputo sin crecimiento en las muestras de las cazoletas de nebulización.

**Conclusiones.** En nuestro estudio no se demostró ninguna infección nosocomial relacionada con el empleo de aerosolterapia en los pacientes con EPOC ingresados por exacerbación aguda.

## INTRODUCTION

Inhaled medications are commonly used for many respiratory diseases. Acute exacerbation of COPD (AECOPD) requires many times aerosolized short-acting beta(2)-agonists every 4

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to 6 hours as part of standard therapy<sup>1</sup>. Nebulized medications are used to accelerate the recovery of patients and they are thought to be safe. However there exists the possibility of nosocomial infections transmitted through nebulized drugs. Reports about nosocomial infections associated with the use of multi-dose bottles<sup>2,3</sup> prompted the centre for disease control (CDC) to elaborate recommendations to avoid these nosocomial infections<sup>4</sup>.

Without absolute adherence to these recommendations when administering inhaled medication, bronchodilator formulations are a potential source of nosocomial infection that can cause morbidity, mortality, and increased hospital costs<sup>5</sup>, especially when treating cystic fibrosis patients and because of intrinsic contamination of drugs nebulization solutions<sup>6,7</sup>. Despite this potential risk little is known regarding nosocomial infections associated to nebulized medications used in AECOPD.

The objective of this study was to evaluate whether the use of nebulized devices can be a source of respiratory infection or not in patients admitted with acute exacerbation of COPD.

## METHODS

Patients consecutively admitted in the Internal Medicine ward with the diagnosis of acute exacerbation of COPD were offered to participate in the study. All patients required nebulized short-acting beta(2)-agonists as standard therapy for AECOPD. Their physician in charge decided treatment administered and the study protocol did not include any medical intervention.

Standard nursery practice included preparation of the nebulized medication at patient's room from single-dose bottles. After its use, facemasks and nebulizers cups were left in the room.

Prior to any use, at day 0, a nebulization with the same characteristic of those used in the patients was held against a blood agar plate (BAP). Another BAP was left open during the nebulization to detect any potential environmental contamination. Samples were repeated on days 4 and 7. Sputum samples were obtained from patients on day 0, prior to any aerosolized medication and on day 7, after the nebulization.

Plates were incubated aerobically at 35°C for 24 hours. If no growth was visible at 24h, plates were incubated for another 24 hours. All colony-forming units were counted and cultured organisms were identified according to CLSI guidelines<sup>8</sup>.

The local Research Ethic Board of our Institution approved the study protocol and every patient signed an informed consent prior to any procedure.

## RESULTS

Forty patients were eligible, 2 patients declined to participate, and 8 were not included because inability to give

informed consent. Thirty patients were finally included. All received short-acting beta(2)-agonists along with other medications. There were 13 men (43%) and median age was 78 years, range 72-86 years. Patients had significant comorbidity (mean Carlson index 5, range 2-8) and 22 of them (73%) had prior admissions for AECOPD in the preceding year. According to GOLD classification<sup>9</sup>, 18 patients were stage IV COPD and 12 were stage III COPD patients. All patients but 4 received antibiotic therapy during admission.

No growth was detected on day 0 and on day 4. After 7 days, BAPs from 9 nebulizations yielded microbiological growth. Coagulase-negative *staphylococci* were the microorganism isolated in all cases. Blood agar plates left open during nebulizations did not retrieve any growth at any time point.

We were able to obtain valid sputum for microbiological culture in all patients at admission with only 6 samples being positive. Microorganisms isolated were *Pseudomonas aeruginosa* (3 patients) *Haemophilus* spp (2 patients) and *Streptococcus pneumoniae* (1 patient). After 7 days of therapy another sputum from 27 patients was sent for culture. Among samples from 27 patients, only three samples yielded bacterial growth, being *P. aeruginosa* the microorganism isolated in all cases. Notably, only one patient with prior *P. aeruginosa* isolation cleared it from sputum. There was a new patient that developed colonization with *P. aeruginosa* during hospitalization, but he had no signs of infection. No patient developed a respiratory nosocomial infection.

## DISCUSSION

In our study we were not able to find any relationship between aerosolized medication and the development of respiratory nosocomial infections in patients admitted for acute exacerbation of COPD.

Although there have been reports about nosocomial infections secondary to the use of aerosolized medication, most of them involved patients with cystic fibrosis and as a result of intrinsic contamination of albuterol bottles<sup>6,10,11</sup>. Other authors have reported cross-contamination among patients with cystic fibrosis using the same facemask and/or the same nebulizer cup as the source of nosocomial infections related to aerosolized medication, although the authors acknowledged that intrinsic contamination could not be completely ruled out<sup>12</sup>.

All these reports have in common that there was not adequate cleaning of facemasks and/or nebulizers cups; the population included, mostly cystic fibrosis patients; and the use of multi-dose bottles, being the latter another potential source of contamination<sup>5</sup>.

To the best of our knowledge, no reports of nosocomial infections in patients with AECOPD related to nebulized medication has been previously reported. COPD patients comprise a group of patients highly susceptible to infections because of frequent comorbidities and long-term use of systemic and inhaled corticosteroids<sup>13</sup> so efforts to reduce the incidence of nosocomial infections in those patients are welcome.

We were not able to establish any relationship between nebulization and nosocomial infections in our patients. After 7 days of therapy there was only growth of CoNS that had no impact on their clinical course. As previously reported<sup>14</sup>, we believe that CoNS represented skin contamination of facemasks used to deliver nebulized medication. We could rule out any significant contribution of environmental contamination with BAPs that were left open close to where facemasks were stored after every use.

In our study we used single-dose bottles that have been related to a reduction in the possibility of nosocomial infections<sup>5</sup>, but facemasks and nebulizers cups were left at patient's room without disinfection after every use. Although not according to CDC guidelines<sup>4</sup>, these practices are well extended in hospital settings. Despite these discrepancies with CDC guidelines we did not had any infection related to aerosolized medication, suggesting a low risk of microbial contamination of nebulizers cups.

We have to acknowledge some limitations of our study; first, sample size might be small, but the fact that none of our patient developed a respiratory infection related to the use of nebulizers suggests that, should they have a role in the epidemiology of nosocomial infections, it is of minimal significance and, second, we must have been unable to detect small amount of pathogenic bacteria. We decided to use Blood agar plates overcome that possibility because they allow growing of fastidious organisms that require rich media. Blood agar plates provide many nutrients and growth factors, so it is unlikely that we had missed any potentially pathogen microorganism.

Our results suggest the absence of any pathogenic role of nebulizer cups in the development of nosocomial infections in COPD patients admitted with acute exacerbation, supporting its perception as a safe practice.

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