

## Maintenance Treatment With Inhaled Ampicillin in Patients With Cystic Fibrosis and Lung Infection Due to Methicillin-Sensitive *Staphylococcus aureus*<sup>☆</sup>

### Tratamiento de mantenimiento con ampicilina inhalada en pacientes con fibrosis quística e infección pulmonar por *Staphylococcus aureus* sensible a metilicina

Dear Editor,

*Staphylococcus aureus* is frequently isolated in the respiratory secretions of patients with cystic fibrosis (CF). Although recent research confirms its pathogenic role in lung inflammation and infection, its optimal treatment has still not been established.<sup>1,2</sup> In this paper, we have studied the effect of nebulized ampicillin in patients with CF and chronic bronchopulmonary infection due to methicillin-sensitive *S. aureus* (MSSA) with poorly-controlled symptoms, frequent exacerbations or respiratory symptoms that are difficult to control with standard treatment (oral or intravenous antibiotics against MSSA during exacerbations).

Thirteen symptomatic patients with CF and chronic bronchopulmonary infection due to MSSA (6 females) were treated with nebulized ampicillin (500 mg/12 h in those weighing under 40 kg and 1 g/12 h in those over 40 kg) 13 symptomatic patients with CF and chronic bronchopulmonary infection due to MSSA (6 females) with a mean age of 14.8±7.6 years (range: 3–34) during a period of time that varied from 6 to 45 months (mean, 23 months). The preparation of nebulized ampicillin was done by diluting a vial of intravenous sodium ampicillin (Gobemycin®, Normon Laboratories, Madrid, Spain) in 4 cc of distilled water or saline solution (or a mix of the two), depending on patient tolerance. A dose of 200 µg of inhaled salbutamol was administered 30 min before nebulized ampicillin. Informed consent was given by the patients and/or their parents. Nebulization was done with compressor systems and nebulizers that are recommended for antibiotics.

A significant reduction ( $P=.033$ ) was observed in the consumption of oral antibiotics after the use of ampicillin (from 28 to 7 days/year). Moreover, hospitalizations also decreased from 4 admittances in the year prior to treatment with ampicillin to just one hospitalization a year ( $P=.046$ ). No statistically significant differences were found for lung function, although it did not decline during the entire treatment period. A reduction was observed in the sputum volume and purulence in all patients. During the treatment with ampicillin, a co-colonization with *Haemophilus parainfluenzae* was detected in the 13 patients. There were no serious adverse effects with the treatment, although 4 patients reported having a bad taste in their mouths after inhaling the antibiotic with distilled water. This bad taste disappeared when the dissolution was made with saline solution or with a mix of serum and water at 50%. During treatment, there was no co-colonization due to *Pseudomonas*

*aeruginosa*, nor was MSSA eradicated. There was an observed great genetic diversity in the MSSA strains (8 clones in 10 patients), with a potential transmission between 2 patients; in the other 8 patients, there was a demonstrated persistence of a single clone without new acquisitions.

The clinical significance of the pathogenic colonization by *S. aureus* in CF patients is still being debated, and there are different therapeutic possibilities.<sup>3</sup> To date, there have been no clinical assays that determined the efficacy and safety of aerosolized antibiotics in chronic bronchopulmonary infection by other different microorganisms of *P. aeruginosa*. Nevertheless, in some patients there has been an observed good response to intravenous antibiotic formulas in CF patients and bronchopulmonary infection due to MSSA and methicillin-resistant *S. aureus*.<sup>4,5</sup>

Although the isolations of MSSA that were analyzed prior to treatment with ampicillin were resistant to penicillin due to the production of penicillinase, the efficacy of treatment in these patients was probably due to the high concentrations of the antibiotic that are reached in the lungs through this treatment pathway, which are higher than CMI for microorganisms that it is directed against.<sup>6</sup>

Although our study has a small number of patients with a varying degree of follow-up, is retrospective and lacks a control group, our results suggest that nebulized ampicillin is safe and improves the control of symptoms in this group of patients.

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