

## SYNOPSIS

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| <b>Title of Study:</b><br>Randomized clinical trial on the evaluation of 2 delayed antibiotic prescription strategies compared to immediate prescription and no antibiotic prescription in uncomplicated acute respiratory infections in primary care (PDA Study)<br><b>EudraCT Number:</b> 2009-011159-29<br><b>Sponsor Protocol Number:</b> PDA  |
| <b>Investigators:</b><br>Pablo Alonso Coello   |
| <b>Study centre(s):</b><br>Iberoamerican Cochrane Center<br>Epidemiology and Public Health Service<br>Hospital de la Santa Creu i Sant Pau   |
| <b>Publication (reference):</b><br>JAMA Intern Med. doi:10.1001/jamainternmed.2015.7088  |
| <b>Studied period (years):</b><br>(date of first enrolment) December 14, 2009<br>(date of last completed) August 28, 2012  |
| <b>Phase of development:</b><br>Phase IV   |
| <b>Objectives:</b><br>The objective of the PDA study was to determine the efficacy and safety of 2 delayed antibiotic prescription strategies, compared with immediate antibiotic prescription and no antibiotic prescription, in the duration and severity of respiratory symptoms in uncomplicated acute respiratory infections.   |
| <b>Methodology:</b><br>Prospective, randomized, open-label, parallel, four-arm multicenter clinical trial.<br>The participants were adults with acute, uncomplicated respiratory infections attended to in 23 primary care centres in Spain.<br>Patients were randomized to 1 of 4 strategies: <ul style="list-style-type: none"><li>- delayed patient-led prescription</li><li>- delayed prescription collection requiring patients to collect their prescription from the primary care center</li><li>- immediate prescription</li><li>- no antibiotic</li></ul> The choice of antibiotic was made by the physician. |
| <b>Number of patients (planned and analysed):</b><br>600 patients Planned, 398 analysed  |
| <b>Diagnosis and main criteria for inclusion:</b><br>Eligible patients were older than 18 years and had 1 of the following acute, uncomplicated respiratory infections: acute pharyngitis, rhinosinusitis, acute bronchitis, or exacerbation of mild-to-moderate chronic obstructive pulmonary disease. In all cases, the physician had reasonable doubt as to whether to treat with an antibiotic.  |
| <b>Test product product, dose and mode of administration:</b><br>Delayed prescription strategies consist of prescribing an antibiotic to take only if the symptoms worsen or if there is no improvement several days after the medical visit.  |

**Reference therapy, dose and mode of administration:**

The choice of antibiotic was made by the physician.

**Main variable**

Duration and severity of symptoms. Patients filled out a daily questionnaire for a maximum of 30 days.

**Secondary variables**

- Antibiotic use
- Satisfaction with health care
- Belief in the effectiveness of antibiotics
- Absenteeism (absence from work or doing their daily activities)
- Risk of complications
- Need for unscheduled health care

**Statistical methods:**

We calculated a sample size of 150 patients per arm (600 patients) considering a mean (SD) of 12 (6) days as the average duration of an acute uncomplicated respiratory infection without treatment. We considered a difference of 2 days in the duration of symptoms in the immediate antibiotic strategy, compared with a delayed strategy, as a clinically relevant result. For our statistical analyses, we used an  $\alpha$  error of 5% ( $\alpha = .05$ ) and a power of 80% ( $\beta = 0.2$ ).

**Summary – Conclusions**

A total of 405 patients were recruited, 398 of whom were included in the analysis; 136 patients (34.2%) were men; mean (SD) age, 45 (17) years. The mean severity of symptoms ranged from 1.8 to 3.5 points on the Likert scale, and mean (SD) duration of symptoms described on first visit was 6 (6) days. The mean (SD) general health status on first visit was 54 (20) based on a scale with 0 indicating worst health status; 100, best status. Overall, 314 patients (80.1%) were nonsmokers, and 372 patients (93.5%) did not have a respiratory comorbidity. The presence of symptoms on first visit was similar among the 4 groups. The mean (SD) duration of severe symptoms was 3.6 (3.3) days for the immediate prescription group and 4.7 (3.6) days for the no prescription group. The median (interquartile range [IQR]) of severe symptoms was 3 (1-4) days for the prescription collection group and 3 (2-6) days for the patient-led prescription group. The median (IQR) of the maximum severity for any symptom was 5 (3-5) for the immediate prescription group and the prescription collection group; 5 (4-5) for the patient-led prescription group; and 5 (4-6) for the no prescription group. Patients randomized to the no prescription strategy or to either of the delayed strategies used fewer antibiotics and less frequently believed in antibiotic effectiveness. Satisfaction was similar across groups.

**Conclusion**

Delayed strategies were associated with slightly greater but clinically similar symptom burden and duration and also with substantially reduced antibiotic use when compared with an immediate strategy.

**Date of report**

December 21, 2015