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LETTER TO THE EDITOR

In response to the article ''Retrospective study on the effectiveness and safety of the shortened 5- to 7 day antibiotic regimen for acute streptococcal pharyngotonsillitis compared to the classic 10-day regimen''

En respuesta al artículo «Estudio retrospectivo sobre la efectividad y seguridad de la pauta antibiótica reducida a 5–7 días en la faringoamigdalitis aguda (faa) estreptocócica comparada con la pauta clásica de 10 días»

Dear Editor:

In response to the article ''Retrospective study on the effectiveness and safety of the shortened 5- to 7 day antibiotic regimen for acute streptococcal pharyngotonsillitis compared to the classic 10-day regimen'' published ahead of print in the journal *Anales de Pediatría* in December 2022 by Salinas Salvador et al.,[1] we would like to comment that shortening the duration of antibiotherapy in acute streptococcal pharyngitis (ASP) is an exceedingly important strategy that should be adequately investigated in Spain given the low incidence of rheumatic fever (estimated at 1/100 000 inhabitants) in developed countries.[2] To this end, in 2020 we developed a phase III non-inferiority trial to assess the efficacy and safety of short amoxicillin courses at the outpatient level in children with ASP, which was awarded the INVEST-AEP grant. This project has been included in the Spanish Register of Clinical Trials (REEC, Registro Español de Ensayos Clínicos; code 2021-004143-24) and has a multicentre design with 4 participating hospitals.

We encountered several challenges in launching this trial, so the start was delayed until next autumn. The first one was the decrease in the prevalence of *S. pyogenes* in Spain—by more than 90% in our hospital—on account of the implementation of hygiene and social distance measures to control the SARS-CoV-2 pandemic. The second was the time required to

Table 1 Inclusion and exclusion criteria for the trial.

Inclusion criteria:
Patient of any sex aged ≥2 years and <18 years.
Patient with a new diagnosis of acute pharyngitis by *S. pyogenes* confirmed microbiologically with the rapid strep test in whom the onset of symptoms occurred at most 72 h before initiation of treatment in the study.
McIsaac score ≥ 2 as long as there is fever with temperature > 38 °C.
Written informed consent provided by the parents or legal guardians in addition to assent provided by patients aged 12 years or older.
Exclusion criteria:
Current antibiotic treatment with an agent whose spectrum covers *S. pyogenes* (penicillin, amoxicillin, amoxicillin-clavulanic acid, macrolides or first-, second- or third-generation cephalosporins).
Treatment in the past 48 h with any of the following drugs: probenecid, alopurinol, tetracyclines, oral anticoagulants or methotrexate.
Recurrent acute streptococcal pharyngitis: 7 or more episodes of acute pharyngitis in the past year, 5 or more episodes a year in the past 2 years or 3 or more episodes a year in the past 3 years. In addition, each of the episodes must meet at least one of the following criteria: purulent tonsillar exudate, temperature > 38 °C, anterior cervical lymphadenitis, isolation of *S. pyogenes* in culture.
Microbiological evidence of acute streptococcal pharyngitis in the 28 days preceding the date of initial care.
Personal history of suppurative and nonsuppurative complications following acute streptococcal pharyngitis.
Personal history of invasive disease (bacteraemia, meningitis) by *S. pyogenes*.
Immunosuppression.
Female patient currently pregnant or lactating.
Follow-up not feasible.
Allergy to amoxicillin.
Parents/legal guardians and/or patient who cannot understand or adhere to all the directions and requirements of the trial.
Based on the judgment of the researchers, the findings of the physical examination, abnormal results of tests or any other medical, social or psychosocial factors suggest that participation could pose a risk to the health of the patient

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Table 2 Schedule and protocol of the trial.

	Baseline	48 h	15 days	4 months
Signed IC	X			
Examination, personal and medical history	X			
Verification of eligibility criteria	X			
Patient enrolment	X			
Random allocation	X			
Physical examination	X			
Vital signs	X			
McIsaac score	X			
Streptococcus pyogenes RDT	X			
Throat swab culture	X			
Administration of amoxicillin	X	X		
Recording any concurrent medication		X	X	
Adverse events		X	X	X
Documentation of temperature		X		
Handing out of journal	X			
Review of journal		X	X	
Recording recurrences			X	
Recording complications			X	X

IC, informed consent; RDT, rapid diagnostic test.

go through administrative processes, that is, the approval of the Clinical Research Ethics Committee and of the Agencia Española del Medicamento y Productos Sanitarios (Spanish Agency of Medicines and Medical Devices). Lastly, economic limitations, despite the award of a grant, as we needed to hire an external company to monitor the data and to conduct drug surveillance of the selected antibiotic agent.

The aim of the trial is to test the hypothesis that shorter courses are not inferior to the conventional course in terms of the incidence of recurrence—reinfection by *S. pyogenes* within 15 days of completing the prescribed course of antibiotherapy—and of suppurative and nonsuppurative complications. Persistent microbiological isolation of *S. pyogenes* will not be interpreted as treatment failure, as the microbe can remain in the pharynx without increasing the risk of complications.[3] In developed countries, rather than eradication, the goal is to reduce the development of antimicrobial resistance[4] by promoting shorter courses.

Table 1 presents the inclusion and exclusion criteria.

Treatment will be given for 5, 7 or 10 days in 3 different groups with a total sample size of 710 patients aged 2–18 years. Table 2 presents the study schedule and protocol. The follow-up will last 4 months from the diagnosis of the acute episode.

The aim of this trial is to confirm the findings described in this article and be able to replace the conventional course by an equally effective course lasting 5 or 7 days.

References

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