Original Paper

Impact of the rapid diagnostic test of *Streptococcus pyogenes* on the consumption of antibiotics in Primary Care

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Abstract

Objective: the aim of the study was to analyse the use of the rapid *Streptococcus* antigen detection test in primary care paediatrics, its impact on antibiotic prescription of and the associated decrease in antibiotic treatment costs.

Material and methods: We conducted a cross-sectional descriptive study in children aged less than 15 years managed in 24 primary care centres between April 2017 and February 2018. We developed a protocol for the use of the rapid strep test (RST). We included patients with a Centor score equal to or greater than 2 points. We collected data on the number of daily defined doses (DDDs) and amount antibiotics prescribed in the study period from the prescription billing system and compared it with the costs corresponding to the previous 12-month period.

Results: 819 TDRS were performed. The results were positive in 250 (30.5%), negative in 557 (68%) and inconclusive in 12 (1.5%). Antibiotics were prescribed to 33% of the patients (all patients with a positive test, 18 with a negative test and 3 with an inconclusive test). Antibiotherapy was not prescribed to 539 of the patients with a negative result (97%). The total number of prescribed DDDs decreased by 21 960 (12%), of which 19 023 (86.6%) corresponded to the most frequently prescribed antibiotics (penicillins, amoxicillin, amoxicillin-clavulanic acid and azithromycin). We found a reduction of €11 320 in antibiotherapy costs (12.5%), while the total cost of rapid testing was € 991, corresponding to total savings of €10 329.

Conclusions: the introduction of the RST in primary care paediatrics has achieved a reduction in the frequency of antibiotherapy. Its use has proven effective in optimising antibiotic use, reducing antibiotic prescription and therefore preventing associated adverse events and reducing unnecessary pharmacotherapy costs.

Key words:
- Cost analysis
- Diagnostic test kit
- Drug utilization evaluation
- Primary care
- *Streptococcus pyogenes*
- Tonsillitis

Impacto en el consumo de antibióticos del test de diagnóstico rápido de *Streptococcus pyogenes* en Atención Primaria

Resumen

Objetivos: analizar el empleo de los test de detección rápida de antígeno estreptocócico en Pediatría de Atención Primaria (AP), su impacto en la prescripción de antibióticos y la reducción de costes del tratamiento antibiótico.

Material y métodos: estudio descriptivo transversal, en menores de 15 años atendidos en AP, en 24 centros de salud, desde abril de 2017 hasta febrero de 2018. Se elaboró un protocolo de utilización del test de detección rápida de antígeno estreptocócico (TDRS). Se incluyeron pacientes con escala Centor mayor o igual a 2 puntos. Se extrajeron del sistema de facturación de recetas datos del número de dosis diaria definida (DDD) e importe de antibióticos en dicha temporada, comparándose con el gasto en los 12 meses previos.

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Palabras clave:
- Amigdalitis
- Análisis de costes
- Atención Primaria
- Evaluación de utilización de fármacos
- Kit de test diagnóstico
- *Streptococcus pyogenes*

Abstract

Resultados: se realizaron 819 TDRS. Resultaron positivos 250 (30,5%), negativos 557 (68%) y 12 no valorables (1,5%). Se prescribió antibiótico al 33% de los pacientes (todos los positivos, 18 negativos, 3 no valorables). En 539 pacientes (97%) con resultado negativo no se instauró antibiótico. El número de DDD total disminuyó en 21 960 (12%), de las cuales 19 023 (86,6%) corresponden a los antibióticos más utilizados (penicilinas, amoxicilina, amoxicilina-clavulánico y azitromicina). La reducción económica fue de 11 320 € (12,5%) y el gasto en TDRS fue de 991 €, lo que supone un ahorro de 10 329€.

Conclusiones: la introducción del TDRS en consultas de Pediatría de AP ha permitido que se eviten un elevado número de tratamientos antibióticos. Su utilización ha demostrado ser eficiente en la optimización del consumo de antibióticos, consiguiendo reducir su utilización, evitar efectos adversos y reducir el gasto farmacéutico innecesario.

INTRODUCTION

Acute pharyngotonsillitis (AP) is one of the most common diseases of childhood and generates up to 30% of paediatric primary care (PC) visits.[1,2] It is more prevalent in countries with temperate climates, with incidence peaks in winter and spring in the northern hemisphere. It is an inflammatory disease of the mucosae of the pharynx or pharyngeal tonsils, manifesting with redness, swelling, exudate, ulcers or vesicles.

The aetiology is usually infectious, most frequently viral (40%-80% of cases), with a self-limiting course and favourable outcomes of disease.[3]

Group A beta-haemolytic streptococcus (GABHS), or *Streptococcus pyogenes*, is the most frequent bacterial causative agent, and is responsible for approximately 15% to 30% of total cases.[4] It is usually detected in patients aged more than 3 years and is rare in younger children (6%-10% of cases of GABHS). However, some authors have reported a prevalence of approximately 20% in infants aged less than 1 year and 26% in children aged 2 to 3 years[5,6] (possibly including asymptomatic carriers, which may account for up to 12% of the total). Thus, despite its low prevalence, some authors recommend performance of diagnostic tests and contemplating the need for treatment in children aged less than 3 years with close contact with cases of AP due to GABHS in the household or at school to decrease the spread of the bacterium and transmission of the disease.[7]

More than 50% of patients with a clinical diagnosis of AP receive empirical antibiotherapy.[4-8] Antibiotic treatment of pharyngotonsillitis caused by GABHS has been generally recommended to reduce the duration of symptoms and to prevent transmission as well as suppurative and nonsuppurative complications of the disease.[8]

However, the clinical presentation of pharyngotonsillitis does not suffice to discriminate between a viral and a bacterial aetiology.[9] Therefore, the purpose of performing diagnostic tests is to be able to make this differentiation. The introduction of rapid antigen detection tests (RADTs) for detection of streptococcus, known as the *rapid strep test* (RST) and easy to perform in the primary care setting, allows early diagnosis and initiation of treatment with a high specificity, and therefore could help reduce unnecessary antibiotic use.

The aim of our study was to analyse the use of the RST in PC paediatric clinics for diagnosis of streptococcal pharyngitis, the impact of this test in antibiotic prescription and the associated reduction in the costs associated with the use of antibiotherapy in these patients.

MATERIAL AND METHODS

We conducted a cross-sectional descriptive study in 34 PC clinics in 24 primary care centres in the Eastern Health District (Área de Salud Este) of Valladolid. The study period ranged from April 2017 to February 2018.

Table 1. Modified/McIsaac Centor Score

Criteria	Score
1. Fever >38°C	1
2. Tonsillar swelling or exudate	1
3. Tender/swollen lateral anterior cervical nodes	1
4. Absence of cough	1
5. Age: • 3-14 years • >14 Years	 1 0
Risk of streptococcal infection (%) • 2%-6% if score = 0-1 • 10%-28% if score = 2-3 • 38%-63% if score = 4-5	

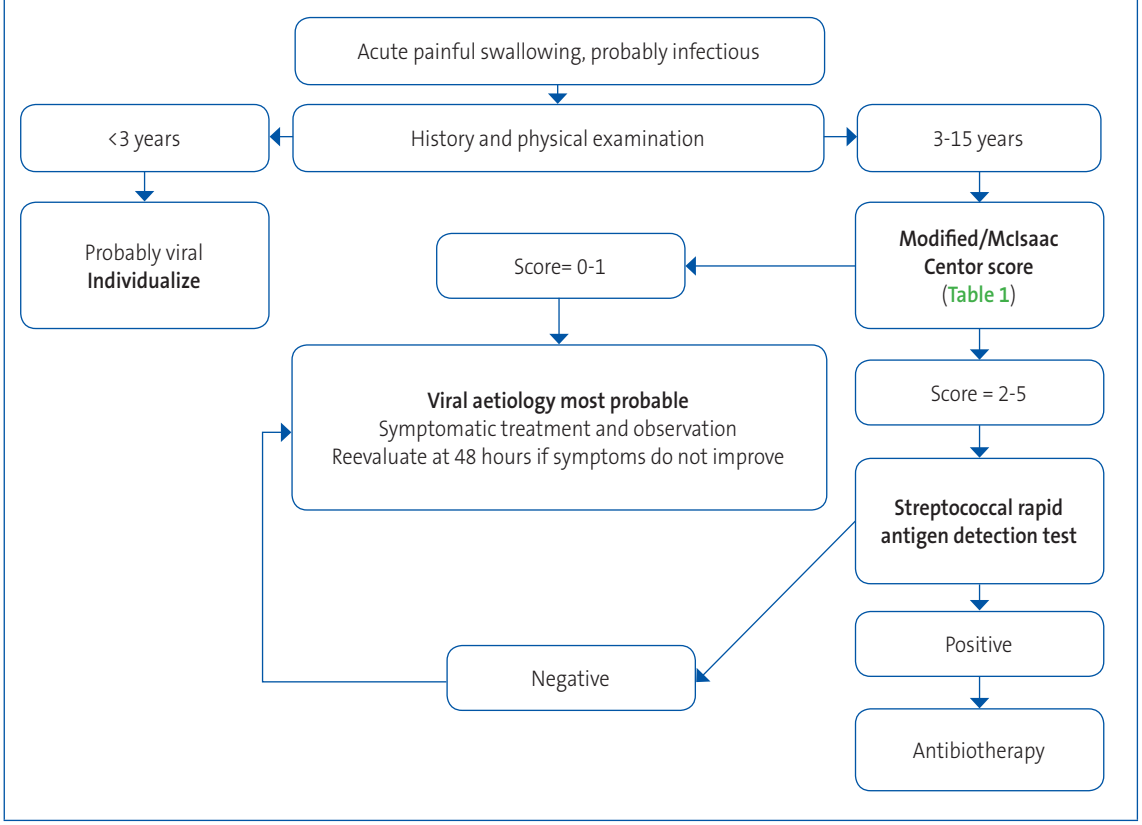
We included all cases of patients aged 14 years or younger that sought care in our clinic for AP of probable streptococcal aetiology. To determine this, we used the Centor score modified by McIsaac (Table 1),[10,11] including all cases with a score of 2 or greater. The exclusion criteria were: Centor score of less than 2, that is, patients with a low probability of having streptococcal pharyngotonsillitis, and additional visits related to the same episode of disease.

We developed a management protocol (Figure 1) based on the age of the patient and the Modified/McIsaac Centor score to select patients that would benefit from performance of a RST and to determine the approach to treatment based on its results.

In the weeks before starting the study, we held training sessions open to all PC paediatricians and nurses and specific trainings in clinics in which we distributed printed documents featuring the indications for antibiotic prescription and directions for correct performance of RSTs.

The study was approved by the Ethics Committee of the Eastern Valladolid health district. After informing families about the study and obtaining

Figure 1. Pharyngotonsillitis management protocol



informed consent, paediatricians performed the clinical evaluation and had a nurse collect a throat swab specimen. The specimen was collected by rubbing a cotton swab on the posterior wall of the pharynx and both pharyngeal tonsils with emphasis on the most reddened areas or areas with exudate, avoiding contact with the tongue, uvula or any other part of the mouth to avoid contamination of the sample with the saprophytic flora of the respiratory tract. The RST was subsequently performed by chromatographic immunoassay (Strep A MonlabTest). The result was available 15 minutes later, and subsequent treatment was administered in adherence with the protocol (**Figure 1**).

We collected data for the following variables: sex, age in years, care setting, signs and symptoms of AP, modified/McIsaac Centor score, use of RST and results, antibiotic prescription and prescribed antibiotic.

We collected data from the CONCYLIA prescription billing system of the Public Health System of Castilla y León (SACYL), documenting the daily defined dose (DDD) and the expenditure in antibiotic prescriptions in the paediatrics sector during the study period, comparing the expenditure with that of the 12 months prior (April 2016-March 2017).

We performed a descriptive analysis of the study variables, expressing quantitative data as mean and standard deviation and qualitative data as absolute frequency and percentage distributions.

RESULTS

We recruited a total of 819 patients with manifestations compatible with acute pharyngotonsillitis and a modified/McIsaac Centor score of 2 or higher. The mean age was 7.5 years (1-14). We found no difference in the presenting signs and symptoms based on age or sex.

The most frequent presenting complaints were fever, painful swallowing and pharyngeal redness or exudate. We found a scarlatiniform rash in 8% of patients. Less frequent manifestations included abdominal pain (1.5%), headache (1.2%) and vomiting (0.6%).

A RST was performed in all patients. The results were positive in 250 (30.5%), negative in 557 (68%) and inconclusive in 12 (1.5%). Four percent of the tests performed corresponded to patients younger than 3 years. In this subset of younger patients, 17.5% had a positive result. The most frequent indication for the RST in this group of patients was the presence of scarlatiniform rash, found in more than half (53%), followed by exudate in the pharynx or tonsils with fever in absence of cough (32%) and fever of unknown origin (15%).

Antibiotherapy was prescribed to 271 patients (33.1%), including all with a positive result of the RST, 18 with a negative result (3.2%) and 3 with inconclusive results (25%). Antibiotherapy was not initiated in 539 patients with negative results (96.8%). Table 2 and Figure 2 present the antibiotic agents used in the sample.

All patients had achieved full resolution of symptoms after completing the course of antibiotherapy, and we did not observe any complications of this treatment.

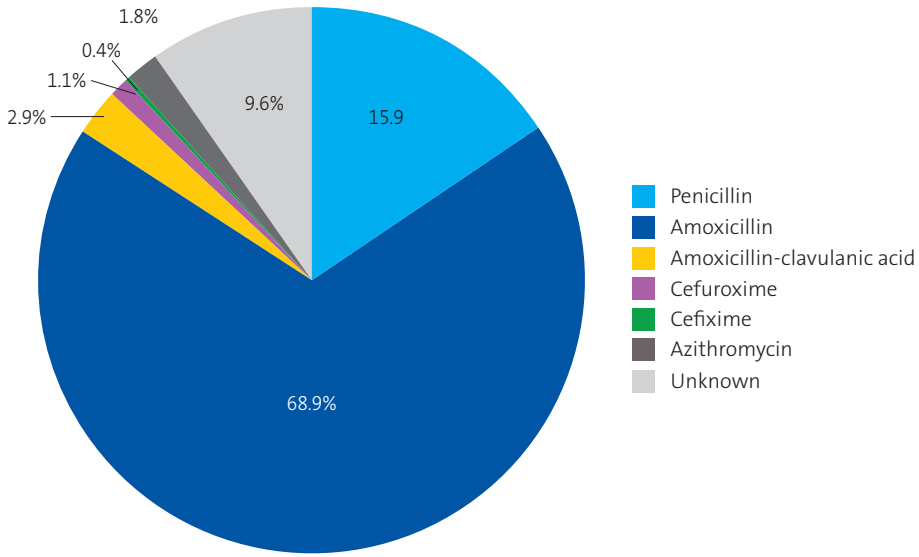
After analysing the prescription database, we found that the number of DDDs in the study period decreased by 21 960 (12%) compared to the same period a year before, of which 19 023 (86.6%) corresponded to the antibiotic agents used most frequently in PC (penicillins, amoxicillin, amoxicillin-clavulanic acid and azithromycin).

The reduction in antibiotherapy costs was €11 320 (12.5%) while the cost of performing RSTs was €991, which resulted in savings of €10 329 in health care costs (11.4%) in our health district.

Table 2. Antibiotic prescription

Antibiotic agent	*n*	Percentage
Penicillin	43	15.9%
Amoxicillin	185	68.9%
Amoxicillin–clavulanic acid	8	2.9%
Cefuroxime	3	1.1%
Cefixime	1	0.4%
Azithromycin	5	1.8%
Unknown	26	9.6%
Total	271	100%

Figure 2. Chart of prescribed antibiotic agents



DISCUSSION

Rapid strep tests are easy to do, yield results in a few minutes in the patient care setting, and allow early and individualised initiation of treatment. This reduces disease transmission and the days of missed school and, above all, optimises antibiotic use. These tests offer a specificity of 95% or higher and a sensitivity that ranges from 70% to 90%[12-18] for diagnosis of AP caused by GABHS. The main drawbacks of this test is that it cannot detect other serotypes and that a negative result does not fully rule out infection by GABHS. In cases in which the RST is negative but there is a high suspicion of streptococcal AP, a throat swab culture could be useful,[19,20] as it has a specificity of nearly 99% and, if the sample has been collected correctly, the sensitivity can be as high as 90% to 95%.[12,21] Although the turnaround time for culture is longer (24-48 hours), this method has the advantage that it can identify different bacteria and serotypes and allows assessment of antimicrobial susceptibility and resistance. Neither test can discriminate between AP caused by GABHS or GABHS carrier status. Nevertheless, given the low prevalence of asymptomatic carriage (ranging from 6% to 12%), antibiotherapy is not recommended routinely in patients with negative results,[3] but only in select cases.[11]

Several scales have been proposed to facilitate diagnosis of AP caused by GABHS and identify patients in who some form of testing is indicated. The one used most frequently is the modified/McIsaac Centor score. This score is based on the presence or absence of certain clinical features, while taking age into account: a body temperature greater than 38°C, tonsillar swelling or exudate, tender swollen anterolateral cervical nodes and absence of cough. It has a high negative predictive value,[22] so that the probability of a positive result in microbiological diagnostic tests is of 3% or less in patients that meet none of the clinical criteria and of 38% to 63% in patients that meet 4 to 5 criteria.[19] Some form of diagnostic testing (RST or culture) is indicated in cases with a score of 2 or greater, unless the clinical presentation were compatible with viral infection, which would invalidate the indication.[23]

The introduction of the RST in the primary care paediatrics setting has allowed to greatly reduce

the prescription of unnecessary antibiotic treatments. As we specified above, the number of total DDDs decreased by 21 960 (12%), of which 19 023 (86.6%) corresponded to the antibiotic agents prescribed most frequently in PC (penicillins, amoxicillin, amoxicillin-clavulanic acid and azithromycin). Our findings were consistent with the previous literature. In 2008, Maltezou *et al*.[24] reported that the use of RSTs achieved a reduction in antibiotic prescription of 61% compared to empirical management of patients based on clinical features. In 2016, Kose *et al*.[25] found that the exclusive use of clinical criteria for diagnosis of streptococcal pharyngotonsillitis led to antibiotic prescription in a high proportion of patients (79.8%), which dropped to 42.6% after performance of rapid testing.

Thus, the use of RSTs in this care setting has proven useful in terms of rational antibiotic use, reducing antibiotic prescription and contributing to preventing the development of drug resistance as well as adverse events.

Another aspect we ought to highlight is that the use of the RST in PC reduces unnecessary drug costs.

Phof *et al*.[26] calculated that the average medical care costs per GABHS case was of $118 (58% of the total cost). Antibiotic treatment amounted to 20% of these costs ($23.60 per case). Kose *et al*.[25] determined that the average cost of empirical antibiotherapy was $7.20 per patient, which decreased by 76.4% ($5.50) with individualisation of treatment following performance of rapid testing. Considering the cost of the RST (of $1.14 per patient), the cost of treatment per patient decreased by 60.6%.

In our study, the reduction in drug prescription costs was of 11 320 € (12.5%), while the costs of rapid testing amounted to €991, with overall savings of €10 329.

In light of all of the above, the use of rapid streptococcal antigen detection tests seems to be an efficient and advisable intervention in primary care paediatrics clinics.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare in relation to the preparation and publication of this article.

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ABBREVIATIONS

AP: acute pharyngotonsillitis • **DDD:** daily defined dose • **GABHS:** group A beta-haemolytic streptococcus • **PC:** Primary Care • **RST:** rapid antigen detection test for streptococcus.

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