

SUPPLEMENTARY MATERIAL

Streptococcal Pharyngitis in Primary Care Pediatrics: Clinical Characteristics, Recurrences, Complications and Antibiotic Management

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Supplementary Materials

Table S1-S6

Supplementary material Table S1. Antibiotic treatment strategies for different clinical presentations of group A streptococcal pharyngitis according to the Italian intersociety consensus (SIPPS-SIP-SITIP-FIMP-SIAIP-SIMRI-FIMMG- SIMG)

Type of GAS infection	Antibiotic therapy	Duration of therapy
Acute Group A streptococcal pharyngitis	First-line therapy: oral amoxicillin 50 mg/kg/day, divided into two doses for 10 days. Intramuscular benzathine-penicillin is reserved for children with impaired intestinal absorption, inability to complete oral therapy, or very high risk of suppurative complications. <u>In cases of suspected but unevaluated amoxicillin allergy</u>, a 5-day course of a third-generation cephalosporin is preferred for low-risk patients. Macrolides are restricted to those with a high risk of severe beta-lactam allergy.	10 days for ARF prevention. A shorter 5–7-day regimens may be considered when the clinical goal is symptom control in low-risk populations
Early* and multiple** clinically recurrences of Group A streptococcal pharyngitis	Amoxicillin for 10 days, or appropriate alternatives in case of allergy. Attention: <u>early recurrences</u> are more likely to represent a true streptococcal infection, whereas <u>multiple recurrences</u> often reflect chronic GAS carriage associated with intercurrent viral infections; in these cases, antibiotic therapy is usually not indicated. In children with multiple recurrences, careful clinical assessment by the primary care pediatrician and appropriate use of rapid antigen detection tests are essential to guide management and avoid unnecessary antibiotic use.	10 days for ARF prevention. A shorter 5–7-day regimens may be considered when the clinical goal is symptom control in low-risk populations
Asymptomatic chronic GAS carrier***	Eradication therapy was considered in children with suspected chronic pharyngeal carriage associated with: - Multiple clinically significant recurrences, defined by <i>Paradise criteria</i>[#], after exclusion of alternative diagnoses - In children's candidates for tonsillectomy because of relapsing pharyngotonsillitis.	Clindamycin for 10 days; or Amoxicillin–clavulanate for 10 days or Amoxicillin for 10 days combined with Rifampicin administered during the last 4 days of treatment.

	In children selected for eradication therapy, the following antibiotic regimens were considered appropriate: • Clindamycin 20–30 mg/kg/day orally in three divided doses for 10 days; or • Amoxicillin–clavulanate 40–50 mg/kg/day (amoxicillin component) orally in two or three divided doses for 10 days; or • Amoxicillin 50 mg/kg/day orally for 10 days combined with rifampicin 20 mg/kg/day orally (maximum 600 mg/day) administered during the last 4 days of treatment.	
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Note: The Supplementary material Table S1 is adapted from the Italian intersociety consensus on the management of pediatric streptococcal pharyngitis (Italian Society of Preventive and Social Pediatrics [SIPPS], Italian Society of Pediatrics [SIP], Italian Society of Pediatric Infectious Diseases [SITIP], Italian Federation of Family Pediatricians [FIMP], Italian Society of Pediatric Allergy and Immunology [SIAIP], Italian Society for Pediatric Respiratory Diseases [SIMRI], Italian Federation of General Practitioners [FIMMG], Italian Society of General Medicine [SIMG]. * Early recurrence of Group A streptococcal pharyngitis is defined as the reappearance of symptomatic streptococcal pharyngitis with positive RADT within a short time after completion of appropriate antibiotic therapy, usually within four weeks. ** Multiple clinically significant recurrences of streptococcal pharyngitis refer to repeated, well-documented episodes of acute streptococcal pharyngitis occurring over months or years, after exclusion of alternative diagnoses and of a chronic carrier state. In the present study, a recurrence — and therefore a new episode — was defined as the reappearance of symptomatic streptococcal pharyngitis with a positive RADT for GAS occurring more than four weeks after completion of antibiotic therapy for the previous episode. *** An asymptomatic chronic GAS carrier was defined in children with persistent pharyngeal colonization by group A Streptococcus, documented by repeated positive throat cultures or rapid antigen tests, in the absence of clinical signs or symptoms of acute pharyngitis, who is unlikely to transmit infection or to develop suppurative or non-suppurative complications. # *Paradise criteria* included at least seven episodes in one year, five episodes per year for two consecutive years, or three episodes per year for three consecutive years

Supplementary material Table S2. Spectrum of acute and chronic complications of streptococcal pharyngotonsillitis and associated antibiotic therapy.

Children with acute/chronic complication of SBEA infection (n=7)							
Acute complication				Chronic complication			
Type of complication	Number of complication	Antibiotic Therapy, dosage	Duration of therapy in days	Type of complication	Number of complication	Antibiotic Therapy	Duration of therapy in days
Peritonsillar/retropharyngeal abscess	1	Amoxicillin-clavulanate 50 mg/kg/die	10	Post-streptococcal glomerulonephritis	1	Amoxicillin-clavulanate 50mg/kg/day	10
Suppurative cervical lymphadenitis	1	Amoxicillin-clavulanate 50mg/kg/die	10				
Sinusitis	1	Amoxicillin 50mg/kg/die	10				
Pneumonia	2	Amoxicillin-clavulanate (1) 50mg/kg/die	10				
		Amoxicillin (1) 50 mg/kg/die	10				
Cellulitis	1	Amoxicillin-clavulanate 50mg/kg die	10				

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Supplementary material Table S3. Distribution of children and episodes of streptococcal pharyngitis according to recurrence status during the observation period

No. of children/No. of episodes 1187/1464	Children who presented with a single episode of streptococcal pharyngitis during the observation period	Children who presented with at least one recurrence of streptococcal pharyngitis during the observation period
No. of first episodes of streptococcal pharyngitis	910/910	277/277
No. of recurrences of streptococcal pharyngitis within four weeks of the previous episode	0	61*/61
No. of recurrences of streptococcal pharyngitis more than four weeks after the previous episode	0	160**/216

Notes:

*61 represents the number of children who experienced a recurrence within 4 weeks of the previous episode of streptococcal pharyngitis and corresponds to the number of episodes.

**160 represents the number of children who experienced 216 recurrences of streptococcal pharyngitis occurring more than 4 weeks after the previous episode; in this case, because some children experienced more than one recurrence, the number of recurrences does not correspond to the number of children

Supplementary material Table S4. Demographic Characteristics, Clinical Features, and Laboratory Findings of Febrile Streptococcal Pharyngotonsillitis Episodes With and Without Complications

Characteristic	Episodes of Febrile Streptococcal pharyngotonsillitis (GAS infection) without development of complications (n=1199)	Episodes of Febrile Streptococcal pharyngotonsillitis (GAS infection) with development of complications (n=7)	<i>p-value</i>
Age			
<5 years	357 (29.8%)	1 (14.3%)	P=0.23
5-8 years	521 (43.5%)	5 (71.4%)	
9-11 years	251 (20.9%)	1 (14.3%)	P=0.40
12-18 years	70 (5.8%)	0 (0%)	P=0.41
Pharyngodinia			
Yes	1152 (96.1%)	6 (85.7%)	<i>p</i> =0.15
No	45 (3.8%)	1 (14.3%)	
Unknown	2 (0.1%)	0	
Pharyngeal hyperemia			
Yes	1150 (97.8%)	6 (85.7%)	<i>p</i>=0.03
No	25 (2.0%)	1 (14.3%)	
Unknown	2 (0.1%)	0	
Tonsillar exudate			
Yes	305 (25.6%)	2 (28.6%)	<i>p</i> =0.85
No	892 (74.2%)	5 (71.4%)	
Unknown	2 (0.1%)	0	
Tonsillar hypertrophy			
Yes	851 (70.9%)	6 (85.7%)	<i>p</i> =0.39
No	346(28.9%)	1 (14.3%)	
Unknown	2(0.2%)		
Palatal petechiae			
Yes	388(32.4%)	2 (28.6%)	<i>p</i> =0.83
No	809 (67.5%)	5 (71.4%)	
Unknown	2(0.1%)		
Strawberry tongue			
Yes	285 (23.9%)	2 (28.6%)	<i>p</i> =0.77
No	912 (76%)	5 (71.4%)	
Unknown	2 (0.1%)		
Lymphadenopathy			
Yes	905 (75.5%)	7 (100%)	<i>p</i> =0.13

No Unknown	292(24.4%) 2 (0.2%)	0 (0%)	
Scarlatiniform rash Yes No Unknown	148 (12.3%) 1049 (87.6%) 2 (0.1%)	2 (28.6%) 5 (71.4%)	$p=0.19$
Gastrointestinal manifestation Yes No Unknown Vomit Diarrhea Abdominal pain	 183 (15.3%) 1014 (84.6%) 2 (0.1%) 106 (8.8%) 15 (1.3%) 102 (8.5%)	 3 (42.9%) 4 (57.1%) 2 (28.6%) 0 1 (14.3%)	 $p=0.04$
Throat swab culture No Yes Positive Negative Antibiotic resistance No Yes Clindamycin Erythromycin Levofloxacin	 1189 (99.1%) 11 (0.9%) 11 (100%) 0 (0%) 7 (0.6%) 4 (0.3%) 1 (0.07%) 2 (0.1%) 1 (0.07%)	 6 (85.7%) 1 (14.3%) 0 (0%) 0 0	 $P<0.001$
Isolated episodes Recurrent episodes	1016 (84.7%) 183 (15.3%)	6 (85.7%) 1 (14.3%)	$p=0.94$
Complication Peritonsillar abscess Lymphadenitis Sinusitis Pneumonia Cellulitis Post-streptococcal glomerulonephritis		 1 (14.3%) 1(14.3%) 1 (14.3%) 2 (28.6%) 1 (14.3%) 1 (14.3%)	

Supplementary material Table S5. Type and duration of antibiotic therapy prescribed for febrile streptococcal pharyngotonsillitis in uncomplicated and complicated cases.

Characteristic	Febrile Streptococcal pharyngotonsillitis (GAS infection) without development of complications (n=1199)	Febrile Streptococcal pharyngotonsillitis (GAS infection) with development of complications (n=7)	<i>p-value</i>
Amoxicillin	907 (75.6%)	2 (28.6%)	P<0.001
10 days	620 (51.7%)	2 (28.6%)	
8 days	7 (0.59%)		
7 days	260 (21.9%)		
6 days	2 (0.17%)		
5 days	14 (1.2%)		
3 days	0 (0.25%)		
2 days	1 (0.08%)		
1 day	3 (0.25%)		
Amoxicillin-clavulanate	158 (13.1%)	5 (71.4%)	
10 days	135 (10.9%)	5 (71.4%)	
8 days	2 (0.17%)		
7 days	18 (1.5%)		
6 days	1 (0.08%)		
2 days	2 (0.17%)		
Other antibiotic therapy	134 (11.2%)	0	
Amoxicillin + Rifampicin	25 (2.1%)		
Amoxicillin-clavulanate+ Rifampicin	2 (0.17%)		
Cefpodoxime proxetil			
10 days	3 (0.25%)		
7 days	7 (0.59%)	0	
3 days	1 (0.08%)		

Cefixime	1 days	1 (0.08%)		
	10 days	33 (%)		
	8 days	7 (0.59%)		
	7 days	8 (0.67%)		
	6 days	1 (0.08%)		
	2 days	1 (0.08%)		
	1 day	2 (0.17%)		
Cefixime + Rifampicin				
	5 days	1 (0.08%)		
Cefaclor				
	8 days	1 (0.08%)		
	7 days	5 (0.42%)		
	5 days	3 (0.25%)		
Azithromycin				
	5 days	4 (0.34%)		
	3 days	9 (0.76%)		
Clarithromycin				
	7 days	3 (0.25%)		
	2 days	1 (0.08%)		
Unknown		6 (0.5%)		

Supplementary material Table S6. Association between scarlet fever manifestations and recurrent streptococcal pharyngitis.

Clinical manifestation	Recurrent streptococcal pharyngitis	No recurrent streptococcal pharyngitis	p-value
Scarlet fever			
	Yes	138 (11.6%)	P<0.001
	No	1049 (88.4%)	
Strawberry tongue			
	Yes	208 (17.5%)	P<0.001
	No	979 (82.4%)	