Treatment of acute pharyngitis in children to prevent rheumatic fever and heart disease

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Description of condition and intervention

Acute pharyngitis is marked by the rapid onset of sore throat, inflammation in pharynx, and fever, and can be of bacterial or viral aetiology. This intervention is targeted only to acute bacterial pharyngitis caused by Streptococcal group A (GAS). The main intention is to prevent rheumatic heart disease, a severe consequence of untreated GAS pharyngitis in children or adolescents (age 5 to 15 years). Presence of discharge, cervical lymphadenopathy, occurrence in winter or spring seasons and absence of cough is suggestive of the former aetiology, with GAS as one of the many causative organisms. GAS pharyngitis is limited to less than one third of all cases of acute pharyngitis and less than 10% of all cases of upper respiratory infection most other causes are viral and do not require antibiotics, so proper differentiation of probable GAS from viral aetiologies is critical to management. Detection of Streptococcal pathogen through diagnostic tests (rapid antigen tests or culture) in primary care settings is useful. Antibiotic therapy is recommended in those who are microbiologically confirmed cases of GAS pharyngitis or history of rheumatic fever. In many low-income settings, laboratory confirmation of GAS is not available or costly, and treatment using a clinical decision rule (Irlam et al 2013) may be more cost-effective. The goal of therapy is to reduce duration and severity of symptoms and any occurrence (or relapse) of rheumatic fever. Treatment regimen of choice for Streptococcal GAS pharyngitis includes oral phenoxymethylpenicillin or amoxicillin for a period of ten days, or, a single intramuscular dose of benzylpenicillin. This evidence brief informs about effectiveness, safety and costs of the treatment of Streptococcal acute pharyngitis. Source: BMJ Best Practice

International guidelines

Organization	Treatment for acute pharyngitis (Streptococcal tonsillopharyngitis)	Applicability in LIC & Lower MIC settings
American Heart Association (2009)	Amoxicillin 50 mg/kg once daily (maximum 1 g) is recommended for 10 days or Benzathine penicillin G 600 000 U for patients ≤ 27 kg (60 lb); 1 200 000 U for patients ≥ 27 kg (60 lb) administered intra-muscular once	Depends upon availability of drugs

Source: Gerber et al 2009

Intervention attributes

Type of interventions

Primary prevention of rheumatic heart disease, focussing on early identification and treatment of GAS pharyngitis. This, in turn, may decrease the risk or relapse of RF in susceptible population. *Source: Watkins et al 2018*

Delivery Platform of intervention

Primary care outpatient setting (Health centre)

Equity

In addition to considerations like cost-effectiveness and health systems factors, dimensions of equity can be relevant for priority setting. The opportunity for a long and healthy life varies according to the severity of a health condition that individuals might have, so there are inequities in individuals' opportunities for long and healthy lives based on the health conditions they face. Metrics used to estimate the severity of illness at an individual level can be used to help prioritize those with less opportunity for lifetime health. FairChoices: DCP Analytics Tool uses Health adjusted age of death (HAAD), which is a metric that estimates the number of years lived from birth to death, discounting years lived with disability. A high HAAD thus represents a disease less severe in terms of lifetime health loss, while a low HAAD represents a disease that is severe on average, causing early death or a long period of severe disability. It is also possible to estimate the distribution of HAAD across individuals with a health condition. FairChoices shows for each intervention an average HAAD value of the conditions that are affected by respective interventions that have health effects. Additionally, a plot shows HAAD values for around 290 conditions (Johansson KA et al 2020).

Time dependence

Moderate level of urgency and treatment outcomes will not be highly affected by some days of delay.

Population in need of intervention

Children, adolescents, and young adults (age 5-24 years) with pharyngitis from GAS infection are the treated population, and it may reduce the incidence rate of rheumatic heart disease of children, adolescents, and young adults (age 5-24 years). In some settings treatment of pharyngitis using a clinical decision rule to assess whether patients have pharyngitis from GAS infection is more cost-effective than testing for GAS, so the population that receives consideration for treatment may be people with pharyngitis.

Intervention effect and safety

Collated evidence of moderate certainty indicates that penicillin treatment reduces incidence or relapse of rheumatic fever and streptococcal throat infections (after 3 days and 1 week), among those with pharyngitis. However, no studies in this evidence summary indicated any effects of penicillin treatment on RHD progression, disability, mortality, or adverse events, among those with sore throat. *Source: Fønhus et al 2021*

Table 1: Effect of penicillin treatment among individuals with acute pharyngitis (from rapid summary by Fønhus et al 2021)

What happens?	No penicillin	With penicillin (95% confidence interval)	Certainty of evidence
Rheumatic fever recurrences Penicillin probably reduces the incidence of acute rheumatic fever within 2 months among people with sore throat (follow up: up to 2 months)	19 per 1 000 people	5 per 1 000 people (3 to 10)	⊕⊕⊕◯ MODERATE
Streptococcal throat infections after 3 days Penicillin probably reduces the number of people with streptococcal sore throat on day 3 among people with sore throat	710 per 1 000 people	405 per 1 000 people (327 to 504)	⊕⊕⊕◯ MODERATE

Model Assumptions

Table 2: Summary of model parameters and values used in FairChoices – DCP Analytical Tool

Category	Model parameter	Notes
Intervention	Treatment of acute pharyngitis	antibiotics with activity against GAS
Cost calculation		
Treated population Incidence of upper respiratory infections		
Gender	Both male & female	
Age	5 to 24 years	
Treated fraction	1	Incidence of upper respiratory infections in 5 to 19 years individuals with sore throat (pharyngitis)
Effect calculation		
Affected population		
Affected gender	Both male & female	
Affected fraction age	5 to 39 years	
Affected fraction	1	Incidence of RHD
Comparison	Other care	
Incidence Reduction (RRR) Strep infections (after 3 days)	0.5	

*Relative risk reduction (RRR) is computed as 1- Relative risk (RR)

Intervention cost

The unit cost is estimated at 2.49 USD per URI case treated, 2019, Kenya (Coates et al 2021). The PIN is calculated based on upper respiratory tract infection incidence, approximately 2.3 cases per year in Sub-Saharan Africa, among children aged 5-14. Based on the "clinical decision rule" with 92% sensitivity and 38% specificity to detect the cases with GAS pharyngitis, estimating that 10% of URI can be attributed to GAS pharyngitis.

Using a population in need based on URI cases, which are about 2-3 in low- and lower-middle-income countries according to GBD estimates, the unit cost per population in need can be derived as follows:

(% of PIN with true positive or false positive GAS strep using clinical decision rule) *(cost of HC visit + cost of treatment) + (% of PIN with true negative or false negative using clinical decision rule) *(cost of HC visit)

(10%*92% + 90%*(1-38%))*(2.37+0.19) + (10%*8% + 90%*38%)*(2.37) = 2.49

References

BMJ Best Practice (https://bestpractice.bmj.com/topics/en-gb/5?q=Acute%20pharyngitis&c=recentlyviewed accessed 24 March 2021)

Irlam et al 2013: Irlam J, Mayosi BM, Engel M, Gaziano TA. Primary prevention of acute rheumatic fever and rheumatic heart disease with penicillin in South African children with pharyngitis: a cost-effectiveness analysis. Circ Cardiovasc Qual Outcomes. 2013 May 1;6(3):343-51. doi: 10.1161/CIRCOUTCOMES.111.000032. Epub 2013 May 7. PMID: 23652737.

Gerber et al 2009: Gerber MA, Baltimore RS, Eaton CB, Gewitz M, Rowley AH, Shulman ST, Taubert KA. Prevention of rheumatic fever and diagnosis and treatment of acute Streptococcal pharyngitis: a scientific statement from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young, the Interdisciplinary Council on Functional Genomics and Translational Biology, and the Interdisciplinary Council on Quality of Care and Outcomes Research.Circulation. 2009; 119:1541–1551. doi: 10.1161/CIRCULATIONAHA.109.191959

Johansson KA, Coates MM, Økland JM, Tsuchiya A, Bukhman G, Norheim OF, Haaland Ø. Health by disease categories. Distributional Cost-Effectiveness Analysis: Quantifying Health Equity Impacts and Trade-Offs. 2020 Sep 30:105.

Watkins et al 2018: Watkins DA, Beaton AZ, Carapetis JR, Karthikeyan G, Mayosi BM, Wyber R, Yacoub MH, Zühlke LJ. Rheumatic Heart Disease Worldwide: JACC Scientific Expert Panel. J Am Coll Cardiol. 2018 Sep 18;72(12):1397-1416. doi: 10.1016/j.jacc.2018.06.063. PMID: 30213333.

Fonhus et al 2021: Fønhus MS and Dalsbø TK. Treatment of sore throat (pharyngitis) to prevent rheumatic heart disease - a rapid summary. 2021. Norwegian Institute of Public Health (NIPH)

Watkins et al 2015: Watkins DA, Mvundura M, Nordet P, Mayosi BM. A cost-effectiveness analysis of a program to control rheumatic fever and rheumatic heart disease in Pinar del Rio, Cuba. PloS one. 2015 Mar 13;10(3): e0121363.

Coates et al 2021: Coates MM, Sliwa K, Watkins DA, Zühlke L, Perel P, Berteletti F, Eiselé JL, Klassen SL, Kwan GF, Mocumbi AO, Prabhakaran D, Habtemariam MK, Bukhman G. An investment case for the prevention and management of rheumatic heart disease in the African Union 2021-30: a modelling study. Lancet Glob Health. 2021 Jul;9(7):e957-e966. doi: 10.1016/S2214-109X(21)00199-6. Epub 2021 May 10. PMID: 33984296.