

RESEARCH ARTICLE

## A Prospective Study of Nonsuppurative Complications of Streptococcal Pharyngitis

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### ABSTRACT

**Objective:** Group A *Streptococci* (GAS) are the most important bacterial cause of pharyngitis. Antibiotic therapy can be prescribed and failure to treat it is associated with suppurative and nonsuppurative complications. Nonsuppurative complications occur after a latency period of a few weeks and include acute rheumatic fever, scarlet fever, streptococcal toxic shock syndrome, acute glomerulonephritis, and pediatric autoimmune neuropsychiatric disorder associated with group A *streptococci*. The aim of this study is to investigate the frequency of nonsuppurative complications in properly treated children with GAS pharyngitis.

**Methods:** We investigated the frequency of nonsuppurative complications in 1030 proven GAS pharyngitis patients between 5 and 15 years old, who were properly treated by a prospective observational study. All patients diagnosed with GAS pharyngitis were followed up prospectively using a standard form for six months made by monthly phone calls.

**Results:** All the isolates recovered from the patients were susceptible to penicillin. Twentyseven (2.6%) patients developed scarlet fever. No other nonsuppurative complications occurred in our patient cohort.

**Conclusions:** Penicillin remains the drug of choice for treatment of GAS pharyngitis. The rate of nonsuppurative complications of GAS pharyngitis has decreased significantly in the antibiotic era. *J Microbiol Infect Dis* 2016;6(1): 8-11

**Key words:** Group A *Streptococci*, nonsuppurative complications, scarlet fever

## Streptokok Faranjitinin Süpüratif Olmayan Komplikasyonlarını İrdeleyen Prospektif Bir Çalışma

### ÖZET

**Amaç:** Grup A Streptokoklar (GAS) faranjitin en önemli bakteriyel nedenidir, çünkü antibiyotiklerle tedavi edilebilir ve tedavi başarısızlığı süpüratif ve nonsüpüratif komplikasyonlara neden olabilir. Nonsüpüratif komplikasyonlar haftalar içinde ortaya çıkan akut romatizmal ateş, kızıl, streptokoksik toksik şok sendromu, akut glomerulonefrit ve Grup A streptokoklara bağlı pediyatrik otoimmün nöropsikiyatrik bozukluğu kapsar. Bu çalışmada uygun antibiyotik tedavisi alan çocuklarda GAS faranjiti sonrası nonsüpüratif komplikasyonların sıklığı araştırıldı.

**Yöntemler:** Bu prospektif gözlemsel çalışmaya 5-15 yaş aralığında İstanbul Medipol Üniversitesi Eğitim ve Araştırma Hastanesinde tanı konulan 1030 kanıtlanmış ve uygun tedavi edilmiş GAS faranjiti dahil edildi. Tanı koyulan tüm olgular standart bir forma kayıt edildikten sonra altı aylık süreyle telefon görüşmeleriyle prospektif olarak izlendi.

**Bulgular:** Hastalardan izole edilen suşların tamamının penisiline duyarlı olduğu saptandı. Olguların 27'sinde (%2,6) kızıl saptanırken, kohortta araştırılan diğer nonsüpüratif komplikasyonlar saptanmadı.

**Sonuç:** GAS faranjiti tedavisinde penisilin halen altın standarttır. Antibiyotiklerin kullanılmaya başlamasıyla nonsüpüratif komplikasyonlarda belirgin azalma gözlemlendi.

**Anahtar kelimeler:** Grup A Streptokoklar, nonsüpüratif komplikasyon, kızıl

### INTRODUCTION

Pharyngitis is the most common clinical manifestation of Group A Streptococcal (GAS) infection. It is most

commonly seen in children between 5 and 15 years of age. 15 to 30 percent of all cases of pharyngitis is the result of streptococcal infection especially during late winter and early spring [1-4].

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Received: 30 April 2015, Accepted: 27 November 2015

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Signs and symptoms of GAS pharyngitis overlap extensively with other infectious causes. Therefore, it is very difficult to make a diagnosis based on clinical findings. In patients with acute febrile respiratory illness, physicians accurately differentiate bacterial from viral infections using only the history and physical findings about one half of the time [5].

GAS pharyngitis is usually a self-limited condition, with symptoms lasting two to five days in untreated patients. Antimicrobial therapy may reduce the duration and severity of symptoms by one to two days in those with positive throat swabs if begun within 2 days of illness [6,7]. Another goal of therapy is to reduce the risk of suppurative and nonsuppurative complications. Rates of suppurative peritonsillar and retropharyngeal abscesses are reduced (approximately one in 1,000 cases) [8]. The incidence of acute rheumatic fever (relative risk reduction =0.28) is also decreased with antibiotics [9].

The aim of this prospective study is to identify nonsuppurative complications of GAS pharyngitis in properly treated patients with positive throat swabs.

## METHODS

### Patient selection and laboratory tests

The study was performed in three private hospitals of Medipol University in Istanbul. From January 2012 to January 2014, all pediatric patients between 5 and 15 years of age who had clinical signs and symptoms of tonsillo-pharyngitis and positive throat cultures for GAS in this prospective observational study. Antimicrobial susceptibility of GAS to penicillin (10 U), erythromycin (15 µg), and clindamycin (2 µg) disks (BBL Becton Dickinson, Sparks, MD, USA) were performed on Mueller-Hinton 5% sheep blood agar plates (MH5BA) (BBL Becton Dickinson, Sparks, MD, USA) by the Kirby-Bauer method. Inhibition diameter zones were interpreted in accordance with the Clinical and Laboratory Standards Institute guidelines (CLSI; M100-S17, 2010) [10].

Ethical approval was given from the institutional ethical committee. Informed consent was given from the patients.

The prescribed antibiotic, dose and duration were recorded on a standard form. A total of 1500 patients were eligible to be followed up prospectively for development of any nonsuppurative complications.

### Clinical data and follow-up

Each patient was called by phone on a monthly basis for 6 months after diagnosis. They were asked

about their current health status, how long they actually took the prescribed antibiotic and to answer a group of questions designed to detect all nonsuppurative complications of GAS pharyngitis. Including acute rheumatic fever (ARF), scarlet fever, streptococcal toxic shock syndrome (STSS), acute glomerulonephritis (AGN), and pediatric autoimmune neuropsychiatric disorder associated with group A streptococci (PANDAS). Only the patients who fulfilled the following criteria were included in the final analysis: 1) ones who received the appropriate antibiotic based on susceptibility testing for the right duration; 2) parents complied fully when called for the questionnaire; 3) accepted a re-examination for further investigation and verification when a complication was suspected [1,11].

## RESULTS

Out of 1500 patients, 1030 (69%) fulfilled the above criteria and were included in the analysis. One-third of the patients were excluded from the study for the following reasons: non-compliance with the drug prescribed, inability to reach by phone, refusal to answer questionnaire. 27 (2.6%) patients were diagnosed with scarlet fever during the follow up period. Details of the patients are given in Table 1. There were no cases with rheumatic fever, streptococcal toxic shock syndrome, acute glomerulonephritis, or PANDAS.

**Table 1.** Demographic characteristics and nonsuppurative complications of the patients.

| Variables                          | No (%)     |
|------------------------------------|------------|
| Mean age                           | 8.82 years |
| 5-10 y                             | 618 (60)   |
| 10-15 y                            | 412 (40)   |
| Male gender                        | 580 (55)   |
| Prescribed antibiotic              |            |
| Aminopenicillin (po)               | 772 (75)   |
| Cephalosporin (po)                 | 104 (10)   |
| Penicillin (im)                    | 42 (4)     |
| Macrolide (po)                     | 104 (10)   |
| Nonsuppurative complications       |            |
| Scarlet fever                      | 27 (2.6)   |
| ARF                                | 0 (0)      |
| Streptococcal toxic shock syndrome | 0 (0)      |
| Acute glomerulonephritis           | 0 (0)      |
| PANDAS                             | 0 (0)      |

PANDAS=pediatric autoimmune neuropsychiatric disorder associated with group A streptococci

None of the isolates were resistant to penicillin and the rates of resistance to erythromycin and clindamycin were 2.2% (33/1500) and 1.8% (27/1500) respectively.

## DISCUSSION

Nonsuppurative complications of GAS pharyngitis occur after a latency period of a few weeks [12]. Not only does the treatment of GAS increase rapid resolution of symptoms, sings and decrease transmission between children; It also prevents the development of ARF when treated within 9 days of the onset of illness [13,14]. The efficacy of penicillin treatment in preventing rheumatic fever is well known. However, duration of penicillin treatment should be for 10 days because shorter durations have shown decreased efficacy [11,15]. Globally, there are 470,000 new cases of rheumatic fever and 233,000 deaths attributable to rheumatic fever or rheumatic heart disease each year. With most occurring in underdeveloped countries and among indigenous groups [16]. The incidence of ARF following streptococcal pharyngitis may be up to 3% and 0.5% in untreated and treated cases, respectively. In developed countries, the incidence of ARF is much lower and likely due to improved hygienic standards and routine use of antibiotics for GAS pharyngitis [17,18]. We have not found any patient with any major manifestations of ARF when choice of treatment complied with the guideline [1,11].

The exact incidence of ARF in Turkey is not known, as the number of reports is not adequate for an accurate estimation. It was estimated as 56.6, 36.7 and 21 per 100,000 children during 1970s, 1980s, and 2000s respectively [19,20]. This decline could be caused by certain factors including increase of antibiotic use, improved hygienic conditions and health services.

According to a recent study from New Zealand, successful reduction of ARF in the community requires a multi-pronged approach, including improving health literacy and addressing socioeconomic determinants, such as household crowding, as well as ensuring GAS pharyngitis is effectively treated [21].

Poststreptococcal glomerulonephritis is induced by infection with specific nephritogenic strains of GAS with an incidence of about 5 to 10 in children infected during an epidemic [22,23]. Although treatment of pharyngitis does not affect the development of poststreptococcal AGN, we have not found any in our 1030 patient [24].

Reasons may be that clinical presentation can vary from asymptomatic, microscopic hematuria to full-blown acute nephritic syndrome. We might have we might have missed subclinical cases and ones with microscopic hematuria [25].

Exotoxin-mediated streptococcal infections may range from localized skin disease to scarlet fever and the rare but sometimes lethal STSS. Scarlet fever, generally evolving from a pharyngeal focus, develops in less than 10% of cases of GAS pharyngitis. 2.6% of our patient cohort developed scarlet fever and none developed STSS.

It is possible that some of our patients were not actually GAS pharyngitis. Since even without treatment, fever and symptoms of the illness may resolve within 3 to 4 days of the onset [14]. Persistence of symptoms beyond this time period suggests either development of a suppurative complication. Or that the patient may be a carrier of GAS (rather than acutely infected), with their presenting symptoms being attributable to an alternate cause of pharyngitis.

The major limitation of our study was that the data provided including duration of therapy was based on statements of the parents. The actual number of patients who complied with treatment may be less. A recent study shows that even though the majority of parents stop administering antibiotics to their children as soon as the symptoms subside, this does not have any apparent negative consequences on complications [26].

## CONCLUSION

Our data shows that penicillin remains the drug of choice for treatment of GAS pharyngitis. In case of documented allergy to penicillin, erythromycin or clindamycin may be considered as an alternative. Our study supports that the rate of nonsuppurative complications of GAS pharyngitis has decreased significantly in the antibiotic era.

**Declaration of Conflicting Interests:** No conflict of interest of any author exists.

**Financial Disclosure:** The authors declared no financial support.

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