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Compliance of patients in medical treatment of pediatric population who has group a beta hemolytic streptococcal pharyngitis in a rural area of Turkey

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Tonsillopharyngitis is a common infectious disease in the pediatric age group. Group A Beta Hemolytic Streptococcus (GAS) is a main infectious agent of pharyngitis. Optimal therapeutic approach in these patients has been a matter of debate to avoid the complications of infection. The aim of this study was to compare the compliance of patients who are 5-15 years old of age groups with tonsillopharyngitis to medical treatment. Six hundred and twenty-two (622) outpatient children who were 5-15 years old and had general infection symptoms as high fever, weakness, chills-shivering and observed hyperemia at tonsils and pharynx were included in the study. Throat culture and antimicrobial susceptibility tests were performed. Compliance of patients to medical treatment was assessed. Seventy-three (11.7%) GAS isolates were obtained from tonsillopharyngeal cultures of the 622 patients. Penicillin, vancomycin, cefepime, erythromycin, chloramphenicol, and clindamycin susceptibility were 100%, 100%, 100%, 98.6%, 98.6%, 98.6% respectively. Compliance of female, male, and all patients to treatment for 5 days were 97.1%, 92.3%, 94.5% respectively and for 10 days treatment, this ratio was respectively 61.7%, 53.8%, 57.5%. To avoid complications of these infections, similar studies should be planned in various places and optimal therapeutic approach must be developed according to socio-economic states of cities and countries.

Key words: *Streptococcus pyogenes*, patients' compliance, medical treatment.

INTRODUCTION

Tonsillopharyngitis is a common infectious disease in the pediatric age group. Group A Beta Hemolytic *Streptococcus* (*S. pyogenes*) (GAS) is a main bacterial infectious agent associated to pharyngitis. Optimal therapeutic approach in these patients has been a matter of debate to avoid the complications of infection. There are some complications of these infections including acute rheumatic fever (ARF), peritonsillar abscess (PTA), and rheumatic heart disease (RHD) (AAP, 2012; VanHowe et al., 2006; Bisno et al., 2002).

Some therapeutic approaches have been identified to

this disease management. Treating the patients with pharyngitis without testing ensures some advantage, but this approach could have some complication such as risk of anaphylaxis, and use of irregular antibiotic has been associated to antibiotic resistance (AAP, 2012; Van Howe et al., 2006). Observing the patients without providing testing or treatments are avoided the risks associated with use of antibiotic, but early treatment with antibiotics may prevent other rare complications of untreated GAS pharyngitis, including PTA, ARF, and RHD (AAP, 2012; Van Howe et al., 2006; Bisno et al., 2002).

Ordering the therapy after testing the patients with pharyngitis with a rapid antigen test, nearly all patients with GAS pharyngitis are identified and treated, but some patients with GAS pharyngitis are missed. If physicians are adequate about test practice, the American Academy of Pediatrics (AAP) and the Infectious Diseases Society of America (IDSA) recommend this approach (AAP, 2012; Van Howe et al., 2006). Performing of throat culture and antibiotics susceptibility tests has the advantage of diagnosis and treatment of GAS pharyngitis cases, but may be delay to initiate the treatment. These approaches are recommended by the Institute for Clinical Systems Improvement (ICSI), the AAP, and the IDSA (AAP, 2012; Van Howe et al., 2006; Bisno et al., 2002; ICSI, 2007). Selecting of antimicrobial treatment of group A streptococcal pharyngitis is an important issues. A number of antibiotics have used for treating group A streptococcal pharyngitis. Penicillin is the drug of choice for treatment of GAS pharyngitis. Erythromycin is alternative for allergic patients to penicillin, and macrolides, cephalosporins, clindamycin can use in therapy. Therapy for 10 days is indicated except for azithromycin (5 days) and penicillin G benzathine (1 dose) (AAP, 2012; Shulman et al., 2012).

The peak age incidence for GAS infections is between 5-15 years olds (Brundage et al., 1996). Acute glomerulonephritis and ARF are nonsuppurative sequelae of GAS disease in these patients. The main goals of antimicrobial therapy for this disease are to reduce morbidity, nonsuppurative sequelae, and transmission to close contacts (AAP, 2012; Van Howe et al., 2006; Shulman et al., 2012).

This study aimed to compare compliance to medical treatment of patients who are 5-15 age groups children with tonsillopharyngitis. It also aimed the research of prevalence of isolated *Streptococcus pyogenes* by bacterial culture analysis from oropharynx microbial flora in these patients, and to determine the susceptibility prevalence of isolated GAS to different groups of antibiotics.

MATERIALS AND METHODS

This study was carried out at the Karaman Karamanoğlu Mehmet Bey Gynecology and Pediatrics Diseases Hospital (Karaman State Hospital) from January till December 2009 in Karaman (Turkey). There has not been any special clinical transaction for this study to the patients and the functioning of the hospital's routine procedures was applied to these patients. Therefore, the approval of the ethical committee has not been considered necessary. Six hundred and twenty-two (622) outpatient children who are 5-15 years old and have general infection symptoms as high fever, weakness, chills-shivering and observed hyperemia at tonsils and pharynx were included in the study. Two hundred and ninety-seven (297) (47.7%) patients were female, and 325 (52.3%) patients were male. Average ages were respectively 9.2 for patients, and 8.9 for females, and 9.5 for males.

During the patients visit, throat swabs were obtained from every patient using transport medium for cultural examination. And then,

antimicrobial therapy for patients who considered GAS pharyngitis was ordered without interfere to choice of medication of physicians as used before this study at this hospital. Three drugs that most commonly used in the hospital were determined. These were penicillin G (penicillin G procaine + penicillin G potassium: 800.000 IU), amoxicillin/clavulanate (45/6.4 mg/kg/day), and clarithromycin (12 mg/kg/day). So, the patients who were ordered one of the three antibiotics were included this study.

The patient's parents were informed about GAS pharyngitis and its complications. It was requested from parents that the antimicrobial therapy should be continued for 10 days. After 15-30 day from first patient's visit, compliance of patients to medical treatment was assessed by interviewing with parents by using telephone or speaking face to face. Statistical analyses were used chi-square test (expected value < 0.05).

After throat swabs were obtained, bacterial cultures were made within 2 h by using the inoculate agar plates containing 5% sheep blood (Oxoid, Hampshire, United Kingdom) and incubated at 37°C for 20–24 h. When the Beta hemolytic colonies were identified on the basis of 10 or more CFU on a blood agar plate, colonies suggestive of β -hemolytic *Streptococcus* were collected and subculture was performed a sheep blood agar slide (5%). Bacitracin disk (0.04 U, Oxoid) and trimethoprim-sulfamethoxazole (25 μ g) disk were placed on the subcultured media. Gram positive, catalase and coagulase negative, susceptible to bacitracin, resistant to trimethoprim-sulfamethoxazole, and β -hemolytic colonies were identified as GAS (*Streptococcus pyogenes*) by using Streptococcal Grouping Kit (Oxoid). The determine of antibiotic susceptibility was performed by disk diffusion technique according to Clinical Laboratory Standards Institute (CLSI) criteria and were tested penicillin (10 unite), vancomycin (30 μ g), erythromycin (15 μ g), chloramphenicol (30 μ g), clindamycin (2 μ g), cefepime (30 μ g) (CLSI, 2008).

RESULTS

In this study, 73 (11.7%) GAS strains was isolated from tonsillopharyngeal cultures of 622 patients, and this bacteria were isolated in 34 (11.5%) of 297 females and in 39 (12.0%) of 325 males. GAS isolates were predominant in October, November and December. Distributions of isolated GAS during the year of study are shown in Figure 1. All isolates were susceptible to Penicillin, vancomycin, and cefepime (30 μ g). A single isolate was resistant to erythromycin, other one to chloramphenicol, and the other one to clindamycin. Susceptibility to Penicillin, vancomycin, cefepime, erythromycin, chloramphenicol and clindamycin was 100%, 100%, 100%, 98.6%, 98.6%, 98.6% respectively.

Compliance on the five days prescribed treatment on females, males, and in all patients was 97.1%, 92.3%, and 94.5% respectively. Compliance on the 10 days prescribed treatment on females, males, and in all patients was 61.7%, 53.8%, and 57.5% respectively. There were not a statistically significant differences in compliance among male and female patients and between antibiotic groups (df=1, $X^2=2.28$, 95% confidence interval; $P < 0.05$). However, compliance among patients receiving 10 days of treatment was lower than those receiving 5 days (df=1, $X^2=19.109$, 95% confidence interval; $P < 0.05$). When the treatment groups were compared, it was not statistically significantly different to

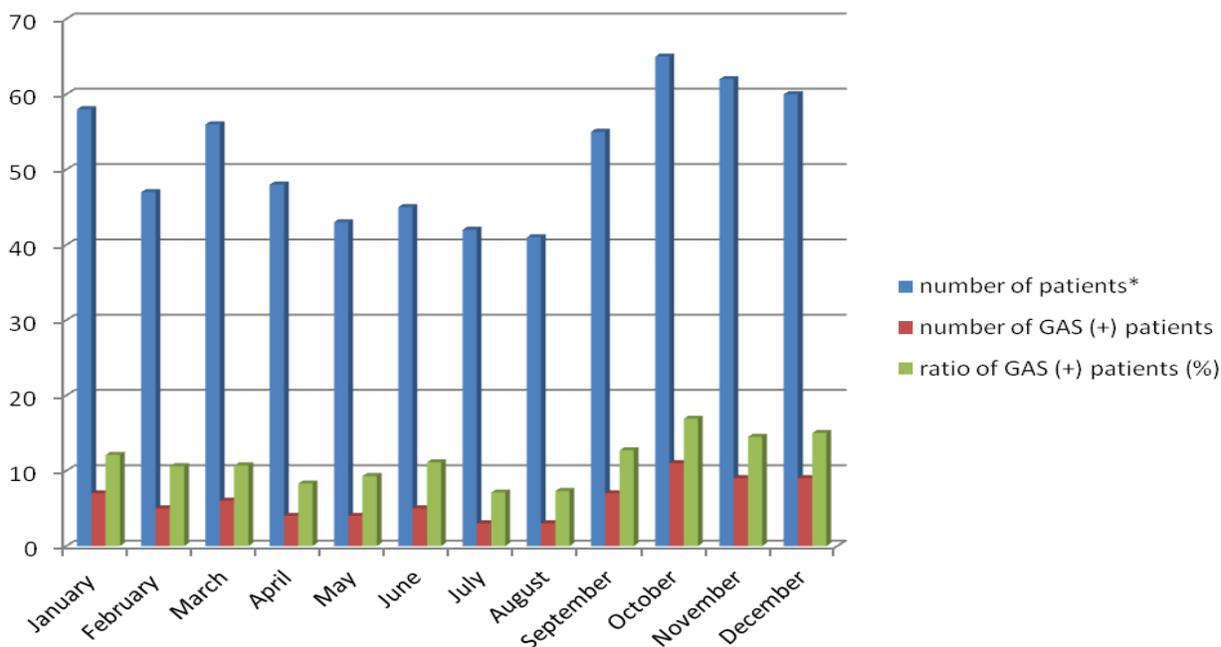


Figure 1. Distributions of isolated GAS during the year of study.

*Number of patients who have general infection symptoms as high fever, weakness, chills-shivering and observed hyperemia at tonsils and pharynx were included in the study.

Table 1. Comparison of compliance of patients who were isolated GAS to medical treatment.

Patient's group	All drugs	Penicillin G	Amoxicillin/clavulanate	Clarithromycin
Distribution of female patients treatment	34	10	11	13
Compliance of female patients to therapy for 5 days: number / %	33/97.1	10/100	10/90.9	13/100
Compliance of female patients to therapy for 10 days: number / %	21/61.7	6/60.0	7/63.6	8/61.5
Distribution of male patients treatment	39	12	12	15
Compliance of male patients to therapy for 5 days: number / %	36/92.3	11/91.7	11/91.7	14/93.33
Compliance of male patients to therapy for 10 days: number / %	21/53.8	6/50.0	7/58.3	8/53.3
Distribution of patients treatment in totally	73	22	23	28
Compliance of all patients to therapy for 5 days: number / %	69/94.5	21/95.5	21/91.3	27/96.4
Compliance of all patients to therapy for 10 days: number / %	42/57.5	12/54.5	14/60.9	16/57.1

adapt the injectable form compared to others ($df=2$, $X^2=5.701$, 95% confidence interval). Comparison of compliance to medical treatment in patients with a GAS isolate is shown in Table 1.

DISCUSSION

Karaman is a small city in rural area in the middle of Turkey. The population of city is approximately 280 thousand and most of the people live in the city center. The majority of people work as a worker in biscuit factories and etc or as an agricultural worker. The 5-15 years old children study in school and they help parents in their task. Karaman Karamanoğlu Mehmet Bey Gynecology and Pediatrics Diseases Hospital that had

128 hospital beds was single place where could be admit to hospital of pediatric patients in those years in Karaman. In daily average, 360 children had been admitted to outpatient to hospital.

GAS infections that cause tonsillopharyngitis are important infectious disease with regard to some complications of these infections in the pediatric age group. The diseases as ARF, RHD, and PTA are serious complications of these infections. Particularly in developing countries, these diseases remain significant public health problems (WHO, 2004). Pharyngitis with GAS and other infections have remained unchanged in both developed and developing countries (WHO, 2004). The clinical microbiology laboratory plays an essential role in rheumatic fever control programs, by facilitating the identi-

identification of GAS infections (WHO, 2004). Nordet et al. (2008) shown that ARF and RHD can be prevented with prevention and control programs of ARF and RHD. To avoid complications of these infections, optimal therapeutic approach must be developed according to socio-economic states of countries.

To be correct of diagnosis of illness is the first step for treatment approach. Performing of throat culture and antibiotics susceptibility tests has the advantage of diagnosis and treatment of GAS pharyngitis cases, and these approaches are recommended by the ICSI, the AAP, and the IDSA (AAP, 2012; Van Howe, 2006; Bisno et al., 2002; ICSI, 2007). In this study, throat culture and antibiotics susceptibility tests were performed. In the performed throat culture, 73 (11.7%) GAS isolates was isolated in the specimen of tonsillopharyngeal swabs of the 622 patients, and this bacteria were isolated in 34 (11.5%) of 297 females and in 39 (12.0%) of 325 males.

Santos et al. (2003) investigated the frequency of GAS infections by rapid test, culture, and gene probe techniques and the culture was observed that the most sensitive test. Omurzakova et al. (2010) compared to rapid antigen detection test and bacterial culture analysis, bacterial culture analysis were observed to be more sensitive test. Morais et al. (2012) reported that the prevalence of GAS were 7.7% (5/65) in the students from a private school. In the performed throat culture study between 1998-2002 years, the percentages of GAS-Positive throat cultures were observed between 13.4% to 17.7% according to study year (Martin et al., 2004). This study referred that the modest increase in the proportion of positive cultures was significantly different when year 3 was compared with years 1 and 4 (Martin et al., 2012). In a performed study, it is informed that throat carriage rates of GAS in spring, summer and winter were 13.0, 8.0 and 16.0%, respectively for children (Danchin et al., 2004). GAS isolates were isolated in 39 (10.15%) of 386 patients who were 5-15 years old in throat cultures by Doğan et al. (2008). Our study is similar to these studies in terms of GAS isolation ratio, and GAS isolation ratio was found higher in autumn and winter than other months. This ratio had begun to rise with the September and had declined in the February. This condition may be explained with that the beginning of school is in September and the school children are on holiday for 15 days in February in Turkey.

In the performed antimicrobial susceptibility tests, susceptibility percentages of penicillin, vancomycin, cefepime, erythromycin, chloramphenicol, and clindamycin were respectively found 100%, 100%, 100%, 98.6%, 98.6%, 98.6%. In the study that performed Pittsburgh, it is reported that no isolate of GAS was determined to be resistant to clindamycin and there were no isolates that were resistant to erythromycin in the first 2 years of the study (Martin et al., 2004). In a comparative study of cefaclor and amoxicillin/clavulanate in pediatric patients with pharyngotonsillitis, all GAS isolates were found be

susceptible to cefaclor and amoxicillin/clavulanate, and be both antibiotics had high and not significantly different eradication ratios at post-therapy (Haczyński et al., 2003). Although all isolates were found susceptible to ampicillin, ceftriaxone, and azithromycin, percentages of resistance of chloramphenicol, tetracycline, and ciprofloxacin were respectively found 19%, 14%, and 12% in a study (Özakkafi et al., 2003). Eryilmaz et al. (2006) reported that all GAS isolates were susceptible to penicillin although ratios of resistance for erythromycin, clindamycin, tetracycline, chloramphenicol were 3.6%, 2.7%, 7.3%, and 0.9% respectively. In a study, it is reported that all GAS isolates susceptible to erythromycin and penicillin (İnan et al., 2003). They reported that all isolates were susceptible to penicillin G, clindamycin, chloramphenicol, cefepime, and vankomycin and an isolate was resistance to erythromycin and another isolate was resistance to ofloxacin (Doğan et al., 2008). In the several study observed that antimicrobial susceptibility ratios are various. Therefore, it is useful to antimicrobial susceptibility testing for the treatment of GAS pharyngitis.

Penicillin is a drug of choice for treatment of GAS pharyngitis and options include cephalosporins, erythromycin, clindamycin, chloramphenicol in penicillin-allergic patients (AAP, 2012; ICSI, 2007; Shulman et al., 2012; WHO, 2004). The effective treatment is 10 days in eliminating the carrier state (AAP, 2012; ICSI, 2007; Shulman et al., 2012; WHO, 2004). A single intramuscular injection of benzathine benzylpenicillin can be choose if it is anticipated that the patient will not adhere to a treatment regimen of oral antibiotics (AAP, 2012; ICSI, 2007; Shulman et al., 2012; WHO, 2004). Azithromycin for 5 days can be chosen to (AAP, 2012; Shulman et al., 2012).

In this study, only medical treatment compliance of patients was observed, the treatment was not directed by researchers. It is observed that the physicians have chosen correct antimicrobial agent when the performed susceptibility tests were analyzed. However, it must be correct from beginning to end of the treatment. Compliance to medical treatment for 10 days was not good. It is observed that compliance to medical treatment for 5 days were better than 10 days treatment. It is reported by AAP (AAP, 2012) that the risk of ARF virtually can be eliminated by adequate treatment of the antecedent GAS infection. Therapy for 10 days is indicated except for azithromycin (5 days) and penicillin G benzathine (1 dose) (AAP, 2012; Shulman et al., 2012). Thus, treatment for 5 days with antimicrobial drugs which used in this study is not sufficient to protect against GAS infections' complications.

Since compliance to medical treatment was not good in this region, alternative therapeutic approaches must be developed. Benzathine benzylpenicillin or azithromycin may be chosen for therapies. Developed therapeutic approaches should be adopted by physicians. Organized educational programs for the public and physicians may

be made. It was not been reached to a similar study about compliance to medical treatment in this topic which made in this region by our review of the literature. It can be requirement to new research in similar topic.

Consequently, this study is limited because of it was performed in a small area locally. To avoid complications of these infections, similar studies should be planned in the various places and optimal therapeutic approach must be developed according to socio-economic states of cities and countries.

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