Journal of Medical Sciences 2023, 4(2) 77-84 **Araştırma Makalesi** / Research Article
https://doi.org/10.46629/JMS.2023.120

The Effect of First Dose Intravenous Antibiotherapy Administered in the Emergency Department on Prognosis in Acute Tonsillopharyngitis Cases

Akut Tonsillofarenjit Vakalarında Acil Serviste Uygulanan İlk Doz İntravenöz Antibiyotiğin Hastalık Seyrine Etkisi

Serdar YAŞAR[1], Ece YİĞİT[2]

SY: 0000-0003-4597-5541 **EY:** 0000-0002-8293-3554

[1] İstanbul Medipol Üniversitesi, Tıp Fakültesi, Acil Tıp Ana Bilim Dalı, Pendik, İstanbul, Türkiye
[2] İstanbul Medipol Üniversitesi, Tıp Fakültesi, İç Hastalıkları Ana Bilim Dalı, Pendik, İstanbul, Türkiye

Abstract

Aim: Streptococcus pyogenes (S.pyogenes) is the most common bacterial cause of acute tonsillopharyngitis in adults. With appropriate and rapid antibiotic treatment, the duration of the disease is shortened, complications are prevented and transmission is reduced. We aimed to determine how the first dose of intravenous (IV) amoxicillin+clavulanic acid treatment administered in our emergency department affects the course of the disease in patients diagnosed with acute tonsillopharyngitis due to S. pyogenes.

Material Method: Patients who applied to our emergency department and internal medicine outpatient clinic with symptoms of upper respiratory tract infection, were positive for streptococcal antigen in the rapid antigen test and scored 2 points or more according to the Centor Criteria were included in our study. Complete blood count and C-reactive protein (CRP) levels were measured at the time of admission and at the end of 72 hours. The patients were divided into two groups: the group who received the first dose of antibiotics as 1000 mg amoxicillin and 200 mg clavulonic acid IV at the time of admission and then used the oral form of the same antibiotic in a 2x1 posology and the group which IV antibiotics were not administered at the time of admission and the same antibiotic was started directly in oral form in the same posology. It was investigated whether there was a significant difference between the leukocyte, neutrophil and CRP levels measured at the end of 72 hours between the two groups.

Results: Age, gender and Centor scores did not show statistically significant differences between the groups. The change

Öz

Amaç: Streptococcus pyogenes (S.pyogenes) erişkinlerde akut tonsillofarenjitin en sık bakteriyel etkenidir. Uygun ve hızlı başlanan antibiyotik tedavisi ile hastalık süresi kısalmakta, komplikasyonlar engellenmekte ve diğer insanlara bulaş azalmaktadır. Çalışmamızda S. pyogenese bağlı akut tonsillofarenjit tanısı koyduğumuz hastalarda acil servisimizde uygulanan ilk doz intravenöz (İV) amoksisilin+klavulonik asit tedavisinin hastalık seyrini nasıl etkilediğini tespit etmeyi hedefledik.

Gereç ve Yöntem: Çalışmamıza acil servisimize ve iç hastalıkları polikliniğimize üst solunum yolu enfeksiyonu semptomları ile başvuran, hızlı antijen testi ile streptokok antijenini pozitif tespit ettiğimiz ve Centor Kriterlerine göre 2 puan ve üzerinde puan alan hastalar dahil edilmiştir. Başvuru anında ve 72 saat sonunda tam kan sayımı ve C-reaktif protein (CRP) düzeyleri ölçülmüştür. Hastalar başvuru anında ilk doz antibiyotiği 1000 mg amoksisilin ve 200 mg klavulonik asit olarak İV olarak alıp sonrasında aynı antibiyotiğin oral formunu 2x1 pozolojide kullananlar ve başvuru anında İV antibiyotik uygulanmamış, aynı antibiyotik aynı pozolojide direkt olarak oral formda başlanmış olanlar olarak ikiye ayrılmıştır. İki grup arasında 72 saat sonunda bakılan lökosit, nötrofil ve CRP düzeyleri arasında anlamlı farklılık olup olmadığı araştırılmıştır.

Bulgular: Yaş, cinsiyet ve Centor skorları açısından gruplar arasında istatistiksel anlamlı farklılık tespit edilmemiştir. Başlangıç anı ve 72 saat sonrası karşılaştırıldığında her iki grupta lökosit, nötrofil ve CRP değerlerindeki değişim istatistiksel olarak anlamlıdır (p <0,001). Gruplar birbiri ile karşılaştırıldığında başlangıç anı ve 72 saat sonrasındaki değişim her üç pa-

* Çalışmamız 24-25 Aralık 2022 tarihlerinde yapılan 11. Uluslararası Tıp ve Sağlık Bilimleri Araştırmaları Kongresinde sözlü bildiri olarak sunulmuştur.

Sorumlu Yazar / Corresponding Author: Ece YİĞİT
E-posta: drece-89@hotmail.com

in leukocyte, neutrophil and CRP values was statistically significant in both groups when the onset and 72 hours were compared (p <0.001). The change between the groups at the beginning and at the end of 72 hours was statistically significantly different for all three parameters (p<0.001).

Conclusion: It was determined that patients who received the first dose of antibiotic treatment IV in our emergency department had a significantly higher decrease in laboratory parameters that had increased due to infection at the end of 72 hours compared to patients who used only oral antibiotics.

Keywords: pharyngitis, anti-bacterial agents, emergency Treatment

rametre için de istatistiksel anlamlı olarak farklıdır (p<0,001).

Sonuç: Benzer klinik durumda olan hastalardan ilk doz antibiyotik tedavisini acil servisimizde İV olarak alan hastaların yalnızca oral antibiyotik kullanan hastalara göre 72 saatin sonunda enfeksiyona bağlı yükselen laboratuvar parametrelerinde anlamlı olarak daha fazla düşüş olduğunu tespit edilmiştir.

Anahtar Kelimeler: farenjit, antibakteriyel ajanlar, acil tedavi

INTRODUCTION

Streptococcus pyogenes (S. pyogenes), a beta-hemolytic bacterium also known as group A Streptococcus (GAS), is the most common bacterial cause of acute tonsillopharyngitis in adults (1). S. pyogenes can cause suppurative complications such as pneumonia, meningitis, and toxic shock syndrome as well as non-suppurative complications such as glomerulonephritis and rheumatic heart disease (2,3). The bacterium, which is highly contagious, can cause illness in healthy people of all ages. The primary transmission route is from person to person through respiratory droplets. More than 616 million new cases of GAS tonsillopharyngitis occur worldwide each year and the disease causes a serious economic burden (4). Complications resulting from rapid invasion of streptococcus into adjacent structures were much more common in the pre-antibiotic period. Today, similar complications are observed in cases where the primary disease is not recognized or the treatment is insufficient due to non-compliance (5). Because it is difficult to distinguish between bacterial and viral infections, the Centor scoring system is used in clinical diagnosis. Higher scores indicate a higher probability of GAS infection (6). On physical examination, the pharynx is erythematous and edematous, the tonsils are enlarged and covered with exudate. It is often accompanied by submandibular and periauricular painful lymphadenopathy. Therefore, patients have difficulty in swallowing and their oral intake may be impaired. Rapid antigen detection tests, which can identify GAS directly from a throat swab, are used to make a quick decision for treatment. In addition, complete blood count, white blood cell count, erythrocyte sedimentation rate, C-reactive protein and procalcitonin are auxiliary laboratory tests that can be used in diagnosis. Throat culture is taken in selected cases (7).

Difficulty in swallowing and non-compliance with oral therapy are frequently observed due to the bacteria's rapid invasion ability, easy transmission, complications and clinical course. Fast and accurate treatment is important for the improvement of the course of the disease, the prevention of possible complications, the reduction of transmission to other people, and thus the decrease in applications to emergency centers and polyclinics with similar complaints (8), which will, in turn, reduce both the cost and the workload on healthcare workers. To date, streptococci causing acute tonsillopharyngitis have remained sensitive to penicillin despite the use of large amounts of beta-lactam. Amoxicillin is one of the beta-lactam antibiotics that is often combined with clavulanic acid. Amoxicillin acts by inhibiting the mucopeptide biosynthesis of the bacterial cell wall. Clavulanic acid, on the other hand, breaks down the beta-lactamase enzyme that bacteria produce to break down beta-lactam in antibiotics to defend themselves and increases the effectiveness of amoxicillin. Therefore, in this study, the aim was to determine how the first dose of intravenous amoxicillin + clavulanic acid treatment administered in the emergency department affected the prognosis of the disease in patients diagnosed with acute tonsillopharyngitis due to GAS.

MATERIAL and METHODS

This was a single-center, prospective, cross-sectional study in which patients who applied to Istanbul Medipol University's emergency department and internal medicine outpatient clinic with symptoms of upper respiratory tract infection between June 2022 and November 2022 were included. Ethical approval was obtained from Istanbul Medipol University's Non-Interventional Clinical Research Ethics Committee (Number: E-10840098-772.02-3124 Date: 01/06/2022). All steps of the study were performed according to the Declaration of Helsinki (originally 1975), as revised in 2008. All patients were informed about the content of the study and their written consent was obtained.

Selection of Participants

Inclusion Criteria:

Patients aged ≥ 18 years

Patients with GAS+ detected by rapid antigen test

Patients with a score of 2 or more according to the Modified Centor Criteria

Exclusion Criteria:

Patients aged <18 years

SARS COV PCR (+) detected patients

Influenza A or B antigens (+) detected patients

Acute or chronic inflammatory disease

Any other acute or chronic infection

Liver dysfunction

Acute or chronic renal failure

Diagnosis of overt diabetes mellitus

Diagnosis of malignancy

Chemotherapy / radiotherapy recipients

Use of immunosuppressive agents

Pregnant and lactating

Medical Examinations

First the medical histories of the patients were taken and demographic data including age, gender and comorbidities were recorded. Detailed physical examinations were performed, then the Modified Centor scores were calculated and recorded. Rapid step antigen tests were performed on all patients. Blood tests including complete blood count and CRP were taken. In addition, swab samples were taken to rule out a possible viral infection due to the epidemic, and the presence of the SARS COV virus and the influenza A / influenza B virus was investigated. The patients were divided into two groups. In the first group, 1000 mg amoxicillin and 200 mg clavulanic acid was prescribed orally in a 2x1 posology without any treatment in the emergency department. In the second group, the first dose of the same antibiotic was administered intravenously at the time of admission, and then the oral form of the same antibiotic was prescribed in a 2x1 posology. At the end of 72 hours, the patients were recalled for control, their physical examinations were repeated, and their complete blood count and CRP values were checked again. It was investigated whether there was a significant difference between the leukocyte, neutrophil, and CRP levels at the end of 72 hours between the two groups.

Randomization

The patients were randomized according to the order of arrival, with patient 1 receiving IV + oral antibiotic therapy, and patient 2 receiving only oral antibiotic therapy.

Calculation of Sample Size

The sample size was calculated according to the results of the pilot study with 20 people. According to the results of this pilot study, the change in leukocyte from before to after was calculated as approximately 1.8 units, the standard deviation of the 1st group was 1.3, and the standard deviation of the 2nd group was 1.6 units. In the study, the sample size of the study was calculated as 12 per group, with Type 1 error α=0.05 and the power of the study at 1-β=80%. The change in neutrophil between groups from before to after was calculated as approximately 1.9 units, with standard deviations of 1.7 and 1.6 units for the Groups 1 and 2, respectively. In the study, the sample size of the study was calculated as 13 per group, with Type 1 error α=0.05 and power of the study at 1-β=80%. The change in CRP between groups from before to after was calculated as 18.3 units, with a standard deviation of 8.6 and 20.7 units for Groups 1 and 2, respectively. In the study, the sample size of the study was calculated as 14 per group, with Type 1 error α=0.05 and power of the study at 1-β=80%. The number of samples was calculated according to the parameter with the

Table 1. Demographic Data

	1st Group	2nd Group	P
Gender	**n**	**(%)**	
Male	22 (44)	22 (45.8)	1.000[1]
Female	28 (56)	26 (54,\.2)	
Age			0.663[2]
Avg±SD	41.8±15.6	43.2±15.3	
Med(min-max)	41(18-84)	39.5(19-76)	
Centor Score			
2	34 (68)	33 (68.8)	
3	15 (30)	12 (25)	
4	1 (2)	3 (6.3)	

[1]Continuity Correction, [2]Fisher's Exact Test, [3]Mann-Whitney U, [2]T-Test

highest sample requirement. Accordingly, the number of samples per group was calculated as 14. It was determined that a minimum of 19 people per group should be included in the study, with a loss supplement of approximately 30%. Sample calculations were performed using the MedCalc Statistical Software version 19.1 (MedCalc Software bv, Ostend, Belgium; https://www.medcalc.org; 2019). A total of 98 patients were included in the present study, 50 patients in group 1 and 48 patients in group 2.

Modified Centor Criteria

Absence of cough is scored as 1 point; painful, enlarged lymphadenopathy is scored as 1 point; fever ≥38 degrees is scored as 1 point; exudate in tonsils is scored as 1 point; between 3-14 years of age is 1 point; between 15-44 years is 0 points; and ≥44 years is -1 point. Higher scores indicate a higher probability of GAS infection (9).

Rapid Strep Antigen Detection Test

Rapid Strep Antigen was studied by immunofluorescence (FIA) method (Device Sofia-Quidel, San Diego, LA, USA).

Laboratory parameters

C-reactive protein was studied using the immunoturbidimetric method (Device Roche Cobas 501 autoanalyzer, Mannheim, Germany).

Complete blood count was studied using an automated hematology analyzer (Device Sysmex XN-1000, Kobe, Japan).

Statistical Analysis

Descriptive statistics were used to describe continuous variables (mean, standard deviation, minimum, median, maximum).

The conformity of continuous variables to the normal distribution was examined using the Shapiro Wilks test.

The relationship between two continuous independent variables that did not conform to the normal distribution was examined with the Mann-Whitney u t test.

The relationship between two continuous dependent variables that did not conform to the normal distribution was examined using the Wilcoxon Signed Rank test.

The relationship between categorical variables was analyzed using the Chi-Square (or Fisher Exact / Yates Continuity-corrected Chi-Square test where appropriate).

The relationship between continuous and dependent variables with normal distribution was examined with the Repeated Measures ANOVA Test.

Statistical significance level was determined to be 0.05. Analyses were performed using the MedCalc® Statistical Software version 19.7.2 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2021) Program.

Table 2. Evaluation of Laboratory Parameters

	Admission	After 72 Hours	Difference	p
Leukocyte Count (10^3/uL)				
1st Group				**<0.001[5]**
Avg±SD	12.5±2.1	10.8±1.6	1.7±1.4	
Med(min-max)	12.6(8.5-17.2)	10.7(7.5-13.9)	1.4(-1.7-4.9)	
2nd Group				
Avg±SD	12.5±1.8	8.7±1.5	3.8±1.4	
Med(min-max)	12.5(9.5-15.7)	8.5(5.7-12.4)	3.6(1.6-6.7)	
p			**<0.001[1]**	
Neutrophil Count (10^3/uL)	**Admission**	**After 72 Hours**		
1st Group				**<0.001[4]**
Avg±SD	9.6±2.1	8.5±1.5	1.1±1.4	
Med(min-max)	9.2(6.5-14.6)	8.4(6.1-11.6)	1.1(-1.3-5.7)	
2nd Group				**<0.001[3]**
Avg±SD	10.1±1.7	6.3±1.4	3.8±1.3	
Med(min-max)	10(7.2-13.6)	6.3(3.7-9.9)	3.9(1.3-6.6)	
p	**0.167[2]**	**<0.001[1]**	**<0.001[2]**	
CRP Level (mg/L)	**Admission**	**After 72 Hours**		
1st Group				**<0.001[3]**
Avg±SD	42±21.2	26.2±14.7	15.8±11.8	
Med(min-max)	41.7(3.1-86.5)	24.5(2.9-64)	13.1(-3.6-51.5)	
2nd Group				**<0.001[4]**
Avg±SD	50.4±18	12.4±8.5	38±14	
Med(min-max)	51.6(8.5-92.5)	11.3(1-35.6)	39.1(6.4-78.5)	
p[1]	**0.037[1]**	**<0.001[2]**	**<0.001[2]**	

[1]Student T-Test, [2]Mann Whitney u test, [3]Paired Sample Test, [4]Wilcoxon Signed Rank test, [5]Repeated Measurements ANOVA

When demographic data are examined, there were no statistically significant differences between groups based on age, gender, and Modified Centor scores (Table 1).

Since the leukocyte values were in accordance with the normal distribution, the repeated measurements were analyzed with the ANOVA Test. The leukocyte value decreased in both groups after the treatment ($p < 0.001$). This regression was greater in the group administered intravenous antibiotics ($p < 0.001$). Neutrophil and CRP values were examined with non-parametric tests since they did not conform

to the normal distribution. Neutrophil and CRP values decreased in both groups before and after treatment ($p<0.001$). This regression was higher in the group using intravenous antibiotics for both parameters ($p<0.001$) (Table 2).

DISCUSSION

This study observed that the first dose of intravenous antibiotic treatment administered before leaving the hospital in patients diagnosed with tonsillopharyngitis due to GAS infection improved the prognosis of the disease. Compared to the group using only oral antibiotics, greater statistically significant regression was observed in leukocyte, neutrophil, and CRP levels after 72 hours.

The normal range for leukocytes is 4000-11000/10^3/uL. Neutrophils, which are subunits of leukocytes, are especially elevated in bacterial infections and the normal range for neutrophils is 1.5-7.1/10^3/uL. High CRP accompanies almost all infections. The normal range for CRP is 0-5 mg/L. In the present study, when all patients were evaluated together, it was found that neutrophil-dominated leukocytosis was found at the time of diagnosis and the CRP value was approximately 8 times higher, in line with this information. The "half-life" of CRP does not change with or without disease, so the "production rate" becomes the determinant of plasma concentration. In case of infection, CRP starts to rise after 4-6 hours and peaks at 36-50 hours. CRP levels are used to understand whether the provided treatment is effective or not, and a control CRP test is often seen at the end of 72 hours. Based on this, patients in this study were recalled for control laboratory tests after 72 hours.

Pharyngitis is one of the most common reasons people go to the hospital for medical care. In the United States, 1-2% of admissions to outpatient clinics and emergency services each year are for sore throat (10). Often the causative agent is viruses, and the infection is self-limited. However, bacterial-viral differentiation is important because unnecessary use of antibiotics in viral infections can lead to antibiotic resistance and disruption of the intestinal flora. Not using antibiotics in bacterial infections will also cause the infection to spread rapidly, contagion, and complications.

Created in 1981 and modified in 2004, the Centor score is a scoring system based on anamnesis and physical examination findings that help determine the decision and approach of antibiotic therapy in cases of tonsillopharyngitis. When the value is ≤0 and 1, the risk of streptococcal infection is considered very low, meaning that further testing and antibiotic therapy are not required. If the value is 2 or 3, it is recommended to perform a rapid antigen test and start antibiotic therapy for any positive results. If the value is ≥4, the risk of streptococcal infection is >50% and empirical antibiotics are recommended (9).

In the guideline published by the Infectious Diseases Society of America (IDSA) for the diagnosis of GAS infection in 2012, it was emphasized that the clinical features of the disease would not be sufficient to distinguish GAS infection from viral pharyngitis causes, and that rapid antigen tests and/or throat culture should be performed. While the IDSA recommends throat culture in children and adolescents with negative rapid antigen test, it emphasized that culture is not needed in adults with negative rapid antigen test (11,12,13).

Rapid antigen tests are specific for GAS. They have the advantage of diagnosing with >95% specificity when performed in patients with a modified Centor score of 2 or higher. Diagnoses were made for the patients within the present study by calculating the modified Centor score and performing a rapid antigen test. All of the patients included in this study were adults, so culture was not required. A critical disadvantage of throat cultures is that results require an extended period of time.

Unfortunately, unnecessary antibiotic use is quite common all over the world as well as in Turkey. One striking study on this topic is an analysis of 3 hospitals in Egypt which found that doctors prescribed antibiotics to 86% of patients with pharyngitis (14). When viewed socially, the large difference between the prevalence of GAS and the rates of antibiotic prescription in patients with pharyngitis increases the economic burden and also causes the development of antibiotic resistance (15,16,17).

The timing of treatment initiation is as important as the treatment approach, which is a point this research sought to emphasize.

One study similar to the present research is a multicenter study conducted on 8168 patients in Taiwan. Patients who applied to the emergency department due to urinary tract infection were divided into two groups: those who received the first dose of intravenous antibiotic therapy in the emergency department and continued oral therapy afterwards and those who received only oral therapy without intrave-

nous therapy. The results of this study showed that the clinical course of patients who received the first dose intravenously in the hospital, similar to the present study, was better and the rate of re-admission to the hospital within 72 hours was lower (18).

A larger study of patients with sepsis demonstrated the importance of hours in initiating antibiotic therapy. 35,000 patients with sepsis who were treated with antibiotics within 6 hours in 21 emergency departments in northern California showed that even one hour of delay in antibiotic administration increased the absolute risk of mortality by 0.3% (19).

From a pharmacokinetic perspective, there is a significant difference in bioavailability between intravenous and oral antibiotics for the treatment of bacterial infections, especially in the early period. With most oral antibiotics, days are required to achieve effective bioavailability (20). For this reason, intravenous antibiotics that reach the peak serum concentration faster are preferred in the treatment of more serious infections (21).

When clinical presentation of the patient group of the present study is examined, tonsillopharyngitis causes nausea, vomiting, cervical adenitis, swelling, and exudate in the tonsils as well as impairs the general condition and oral intake, and all of these may cause incompatibility in oral antibiotic therapy. For this reason, administering the first dose of antibiotics intravenously may increase the rapid elimination of bacteria, the improvement of the general condition of the patient, and the compliance with the treatment. Antibiotics are known to be most effective in tonsillopharyngitis when started in the first 48 hours, and contagiousness disappears within 24 hours after antibiotics are started. Therefore, it may be a logical option to administer the first dose of antibiotics intravenously in the emergency room, both on an individual patient basis and socially.

Limitations

The present study was a single-center study conducted on 98 patients. Multicenter studies with more patients are needed. In addition, the cause-effect relationship cannot be established clearly due to the cross-sectional nature of this study.

CONCLUSION

This research determined that patients with similar clinical conditions who received the first dose of antibiotic treatment in an emergency department had a significantly higher decrease in laboratory parameters, which increased due to infection, at the end of 72 hours, compared to those who were provided only oral antibiotics. It seems like a good option to administer the first dose of antibiotic therapy in the emergency department, both because oral intake can be impaired in the initial phase and patient non-compliance with the treatment and the bioavailability of intravenous antibiotics is improved.

Received/Geliş Tarihi: 17.02.2023
Accepted/Kabul Tarihi: 24.04.2023

REFERENCES

1. Schroeder BM. Diagnosis and management of group A streptococcal pharyngitis. American family physician. 2003;67(4): p. 880.
2. Stevens DL. Streptococcal toxic-shock syndrome: spectrum of disease, pathogenesis, and new concepts in treatment. Emerging infectious diseases.1995;1(3): p. 69.
3. Mani R, Mahadevan A, Pradhan S, Nagarathna S, Srikanth NS, Dias M, et al. Fatal Group A Streptococcal meningitis in an adult. Indian J Med Microbiol. 2007;25(2):169-70.
4. Carapetis JR, Steer AC, Mulholland EK., Weber M. The global burden of group A streptococcal diseases. The Lancet infectious diseases. 2005;5(11): p. 685-694.
5. Callister ME, Wall RA. Descending necrotizing mediastinitis caused by group A streptococcus (serotype M1T1). Scandinavian journal of infectious diseases. 2001; 33(10): p. 771-772.
6. Maltezou HC, Tsagris V, Antoniadou A, Galani L, Douros C, Katsarolis I, et al. Evaluation of a rapid antigen detection test in the diagnosis of streptococcal pharyngitis in children and its impact on antibiotic prescription. Journal of antimicrobial Chemotherapy. 2008;62(6): p. 1407-1412.
7. Dhanda V,Vohra H, Kumar R. Virulence potential of Group A streptococci isolated from throat cultures of children from north India. The Indian Journal of Medical Research. 2011;133(6): p. 674.
8. Gerber MA, Randolph MF, DeMeo KK, Kaplan EL. Lack of impact of early antibiotic therapy for streptococcal pharyngitis on recurrence rates. The Journal of pediatrics, 1990;117(6): p. 853-858.
9. Centor RM, Witherspoon JM, Dalton HP, Brody CE, Link K. et al. The

diagnosis of strep throat in adults in the emergency room. Medical Decision Making. 1981;1(3): p. 239-246.

10. Prevention CfDCa. National Hospital Ambulatory Medical Care Survey: Emergency Department Summary Tables 2017. https://www.cdc.gov/nchs/data/nhamcs/web_tables/2017_ed_web_tables-508.pdf

11. Shulman ST, Bisno AL, Clegg HW, Gerber MA, Kaplan EL, Lee G, et al. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. Clinical infectious diseases. 2012;55(10): p. e86-e102.

12. Sheridan EJ, Ludwig J, Helmen J, Thevatheril IT. Should you treat a symptomatic patient by phone when his child has confirmed strep throat? J Fam Pract. 2007;56(3):234-5.

13. Cooper RJ, Hoffman JR, Bartlett JG, Besser RE, Gonzales R, Hickner JM, et al. Principles of appropriate antibiotic use for acute pharyngitis in adults: background. Annals of internal medicine, 2001; 134(6): p. 509-517.

14. Langlois DM, Andreae M. Group A streptococcal infections. Pediatr Rev, 2011. 32(10): p. 423-9; quiz 430.

15. Ahmed MH, Hassan MF, Eida MM, Metwally LA. Evaluation of Appropriateness of Antibiotic Use and Validation of the Mclsaac-Modified Centor Score for Group A Beta Hemolytic Streptococcal Acute Pharyngitis in Suez Canal Area. Suez Canal University Medical Journal. 2015;18(2): p. 117-124.

16. Humair JP, Revaz SA, Bovier P, Stalder H. Management of acute pharyngitis in adults: reliability of rapid streptococcal tests and clinical findings. Archives of Internal Medicine. 2006;166(6): p. 640-644.

17. Neuner JM, Hamel MB, Phillips RS, Bona K, Aronson MD. Diagnosis and management of adults with pharyngitis: a cost-effectiveness analysis. Annals of internal medicine. 2003;139(2): p. 113-122.

18. Linder JA, Stafford RS. Antibiotic treatment of adults with sore throat by community primary care physicians: a national survey, 1989-1999. Jama. 2001;286(10): p. 1181- 1186.

19. Poh XE, Wu KH, Chen CC, Huang JB, Cheng FC,Chiu IM. Outcomes for Patients with Urinary Tract Infection After an Initial Intravenous Antibiotics Dose Before Emergency Department Discharge. Infectious Diseases and Therapy. 2021;10(3): p. 1479-1489.

20. Liu VX, Fielding-Singh V, Greene JD, Baker JM, Iwashyna TJ, Bhattacharya J, Escobar GJ. The Timing of Early Antibiotics and Hospital Mortality in Sepsis. Am J Respir Crit Care Med. 2017;196(7): p. 856-863.

21. van den Broek AK, Prins JM, Visser CE, van Hest RM. Systematic review: the bioavailability of orally administered antibiotics during the initial phase of a systemic infection in non-ICU patients. BMC infectious diseases. 2021;21(1): p. 1-11.

22. Huang YH, Yan JH, Kuo KC, Wu WT, Su CM, Chiu IM. et al. Early antibiotics use in young infants with invasive bacterial infection visiting emergency department, a single medical center's experience. Pediatrics & Neonatology. 2020;61(2): p. 155-159.