

Effect of chlorhexidine gluconate and benzydamine hydrochloride mouth spray on clinical signs and quality of life of patients with streptococcal tonsillopharyngitis: multicentre, prospective, randomised, double-blinded, placebo-controlled study

C CINGI¹, M SONGU², A URAL³, N ERDOGMUS¹, M YILDIRIM⁴, H CAKLI¹, C BAL⁵

Departments of ¹Otorhinolaryngology and ⁵Biostatistics, Osmangazi University Medical Faculty, Eskisehir, ²Department of Otorhinolaryngology, Izmir Ataturk Research and Training Hospital, Izmir, ³Department of Otorhinolaryngology, Karadeniz Technical University Medical Faculty, Trabzon, and ⁴Department of Otorhinolaryngology, Dicle University Medical Faculty, Diyarbakir, Turkey

Abstract

Objective: To assess the effect of chlorhexidine gluconate and benzydamine hydrochloride mouth spray, used in conjunction with antibiotic treatment, on the intensity of clinical signs and quality of life of patients with group A streptococcal tonsillopharyngitis.

Methods: Patients ($n = 147$) with streptococcal tonsillopharyngitis were recruited and randomly allocated to either the treatment group (penicillin plus chlorhexidine and benzydamine; $n = 72$) or control group (penicillin plus placebo; $n = 75$). Blinded assessments were conducted before and after 10 days' treatment, using an intensity rating scale for clinical sign severity, a visual analogue scale for subjective health state, the Short Form 36 Health Questionnaire for quality of life, and a customised questionnaire for side effects.

Results: The treatment group showed a statistically significant reduction in the intensity of clinical signs, compared with the control group. On treatment day 7, there was no significant difference in quality of life between the treatment and control groups. The treatment drugs were well tolerated, and no serious adverse events were observed.

Conclusion: Chlorhexidine gluconate and benzydamine hydrochloride mouth spray, added to standard antibiotic treatment, significantly alleviate the intensity of clinical signs in patients with streptococcal pharyngitis. Further research is needed using larger sample sizes or alternative control groups.

Key words: Pharyngitis; Tonsillitis; Chlorhexidine; Benzydamine; Therapeutics

Introduction

Acute tonsillopharyngitis, characterised by inflammation of the oropharyngeal cavity and surrounding lymphoid tissue, is one of the most common diseases encountered by general practitioners and otorhinolaryngologists.¹ Tonsillopharyngitis is caused by *Streptococcus pyogenes*, a highly virulent, group A β -haemolytic streptococcus, in 5–30 per cent of patients.² Accurate detection of the causative organism is useful in order to plan correct treatment (avoiding unnecessary wide-spectrum antibiotics) and to prevent complications. Although throat swab culture is the 'gold standard' for tonsillopharyngitis diagnosis, it takes 24–48 hours to obtain the result. Rapid antigen

detection is a quick and reliable alternative which can be used for the diagnosis of group A streptococcal tonsillopharyngitis.

In cases of recurrent sore throat associated with group A β -haemolytic streptococcus, a 10-day course of antibiotics may reduce the number and frequency of attacks.³ However, treatment of a sore throat with antibiotics has only a modest beneficial effect on clinical signs, including fever.^{4,5} Numerous pharmaceutical preparations are available, containing disinfectants, anti-inflammatory agents and/or topical anaesthetics, which may potentially provide symptomatic relief.³

The present study aimed to investigate the effect of a mouth spray containing chlorhexidine gluconate and

benzylamine hydrochloride, in comparison with placebo, on the intensity of clinical signs and the quality of life of patients with streptococcal tonsillopharyngitis, using a prospective, randomised, double-blinded, placebo-controlled trial.

Materials and methods

Study design

This study was designed as a multicentre, prospective, randomised, double-blinded, placebo-controlled, parallel-group clinical trial. The study was undertaken between May and October 2009.

The study protocol was approved by the relevant ethics committee, and a completed written consent form was obtained from each patient.

The study was conducted in the ENT clinics of three university hospitals and one tertiary hospital.

Rapid antigen detection test

The rapid antigen detection test ('rapid strep test') is a quick and accurate diagnostic tool used to determine the presence of streptococcal bacteria. Results can be obtained within minutes to hours. In our study, a sample of throat mucus (obtained from the surface of the palatine tonsils using a swab) was tested for group A streptococcal bacteria using the QuickVue Dipstick Test (Quidel, San Diego, California, USA).

Study protocol

We enrolled in the study patients of both genders who were admitted with clinical signs of acute tonsillopharyngitis and who had a positive streptococcal A antigen test result. The study's inclusion and exclusion criteria are shown in Table I.

One hundred and seventy-one patients, encountered at four study centres, were randomised in a double-blinded manner to receive one of two parallel treatments: penicillin V plus active drug mouth spray, or

penicillin V plus placebo mouth spray. The active drug mouth spray contained chlorhexidine gluconate 0.12 per cent and benzylamine hydrochloride 0.15 per cent; the placebo mouth spray contained no active ingredients. Patients used their mouth spray four times per day, and were instructed to avoid taking any other medications for the relief of sore throat.

Treatment randomisation was generated by the study coordinator (CC, the senior author), using a numbered list of patients, prior to study commencement. Numbered boxes containing either treatment or placebo were sent to the clinical investigators. Each box's number was noted on the appropriate patient's questionnaire. The clinical investigators at the four study centres were thus blinded to whether individual patients had received mouth spray containing active treatment or placebo. Two copies of the randomisation codes determining each patient's treatment were stored in two sets of sealed envelopes. One set of envelopes was kept by the study coordinator, while the other set was distributed amongst the study centres in case of emergency (i.e. in the event that knowledge of the patient's actual treatment were to become medically necessary). Revealing the randomisation code for one patient would not require other patients' codes to be revealed. In this way, all investigators and patients were blinded to treatment assignment throughout the course of the study.

Outcome measures

Intensity of clinical signs. Investigators assessed the intensity of patients' clinical signs prior to treatment and on the seventh day of treatment. The assessed clinical signs comprised included sore throat, erythema and oedema of the posterior pharynx, exudate, cervical lymphadenopathy, and headache. These were graded on a four-point scale (with 0 = absent, 1 = mild, 2 = moderate and 3 = severe), and an overall clinical sign score was generated. Investigators were provided with reference guidelines to aid their classification of clinical sign intensity (see Appendix 1).

Subjective health state. Patients were asked to subjectively assess their health state using a 10 cm visual analogue scale (VAS) graded from zero (representing 'the best imaginable health state') to 10 ('the worst imaginable health state').⁶ Patients completed a VAS before treatment and on the third and seventh days of treatment. This information was used as a quantitative measure of patients' individual, subjective health outcome.

Quality of life. Patients completed the Short Form 36 Health Questionnaire before treatment and on the seventh day of treatment. This questionnaire (comprising a short form with 36 questions) is a well documented, self-administered, simple, standardised quality-of-life scoring system which has been widely used and validated.^{7,8} The questionnaire contains eight independent scales summarised into two 'dimensions': the physical

TABLE I
INCLUSION AND EXCLUSION CRITERIA

<i>Inclusion criteria</i>
Age over 15 and under 65 years
Sore throat for 2–7 days
Positive rapid antigen detection test
Able to understand and give written, informed consent, and to report adverse events and concomitant medication for duration of study
<i>Exclusion criteria</i>
Sore throat for more than 7 days
Any medication* taken for sore throat relief prior to study initiation
Concurrent analgesic or anti-inflammatory regimen requiring treatment with analgesics, NSAIDs or steroids
Clinical signs of sore throat caused by local irritation of mucous membranes due to gastroesophageal reflux or ingestion of caustic substances
Pregnancy, or inadequate contraception in woman with child-bearing potential

*Including herbal medicine or dietary supplements. NSAIDs = non-steroidal anti-inflammatory drugs

health dimension and the mental health dimension. Each dimension includes three specific and two overlapping scales. The questionnaire also includes a question on self-evaluated change in health during the past year ('reported health'); this question is scored independently. Scores for the two dimensions, and the total score, are based on mathematical averaging of scale component scores.

Side effects. Patients used a customised questionnaire to assess any side effects of treatment. This questionnaire was completed on the third and seventh days of treatment. A four-point Likert scale was used to assess local side effects (e.g. taste disturbance, oral mucosal numbness, oral burning sensation, dry mouth or thirst, and tooth discolouration) and systemic side effects (e.g. nausea, vomiting, dyspepsia, vertigo and headache), with 0 = none, 1 = mild, 2 = moderate and 3 = severe.

Statistical analysis

Data were analysed using the Statistical Package for the Social Sciences version 17.0 for Windows (SPSS Inc, Chicago, Illinois, USA). Shapiro–Wilk's test was used to test the normality assumption. Paired samples were analysed using Student's *t*-test, while repeated measures were analysed using one-way analysis of variance. Values were expressed as mean \pm standard deviation. Statistical significance was accepted for *p* values less than 0.05.

The distribution forms for the data were determined using Shapiro–Wilk's test; all data were found to fit a normal or Gaussian distribution. In our study, the power of parametric testing was found to be greater than that of nonparametric testing. When performed with a value of $\alpha = 0.050$, the testing power was found to be >0.80 ; this level of power was considered sufficient.

Results

We evaluated a total of 171 patients selected according to the study inclusion criteria. Sixteen patients did not complete the trial, and eight were excluded in the follow-up period. Thus, 147 patients remained enrolled in the study: 72 females (mean age 38.92 ± 14.38 years) and 75 males (mean age 36.73 ± 17.61 years). All patients used their medication as directed, and none took additional medication. Following study termination, 72 patients were found to have been assigned to the penicillin V plus treatment group, while 75 had been assigned to the penicillin V plus placebo group. The two groups had similar age and sex distributions ($p = 0.413$ and $p = 0.367$, respectively).

Intensity of clinical signs

Prior to treatment, there was no significant difference in patients' clinical sign intensity scores, comparing the treatment and control groups ($p = 0.403$).

At the end of the treatment period, however, there was a significant difference in clinical sign intensity scores between these two groups ($p < 0.001$)

TABLE II
CLINICAL SIGN INTENSITY SCORES PRE- AND POST-TREATMENT

Time point	Score
<i>Treatment group</i>	
Pre-treatment	12.86 \pm 1.76
Post-treatment	3.12 \pm 0.97
<i>Control group</i>	
Pre-treatment	13.08 \pm 1.60
Post-treatment	6.07 \pm 1.56

Data represent means \pm standard deviations.

(Table II). Clinical sign scores significantly reduced over time in both the treatment and control groups ($p < 0.001$ for both). However, this reduction was significantly greater in the treatment group than in the control group ($p < 0.001$; Figure 1).

Subjective health state

Before treatment, there was no significant difference in patients' VAS scores for subjective health state, comparing the treatment and control groups ($p = 0.928$).

However, following treatment initiation, a significant difference in VAS scores was seen between the treatment and controls groups, on both the third and seventh days of treatment ($p < 0.001$ and $p < 0.001$, respectively) (Table III, Figure 2).

Quality of life

Analysis of Short Form 36 Health Questionnaire quality-of-life scores on the seventh day of treatment revealed no statistically significant difference between treatment and control groups ($p > 0.05$; Table IV, Figure 3). A significant improvement in quality-of-life scores was seen over time in both the treatment and control groups ($p < 0.001$ for both).

Side effects

Analysis of side effects in the treatment and control groups revealed a statistically significant difference

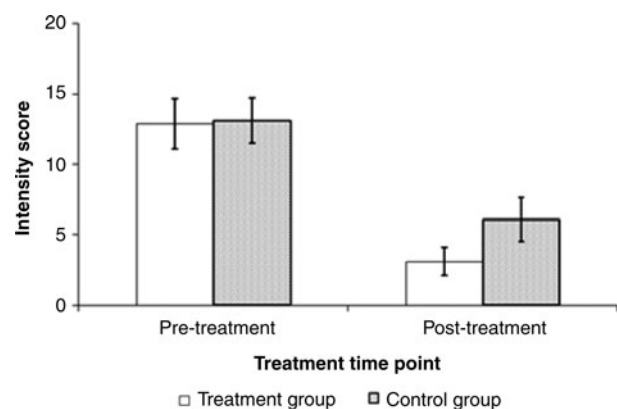


FIG. 1

Clinical sign intensity scores for treatment and control groups, pre- and post-treatment.

TABLE III
VAS SCORES FOR SUBJECTIVE HEALTH STATE
PRE- AND POST-TREATMENT

Time point	Score
<i>Treatment group</i>	
Pre-treatment	7.47 ± 1.46
Treatment day 3	4.13 ± 1.16
Treatment day 7	2.78 ± 1.06
<i>Control group</i>	
Pre-treatment	7.45 ± 1.48
Treatment day 3	5.52 ± 1.21
Treatment day 7	3.96 ± 1.36

Data represent means ± standard deviations. VAS = visual analogue scale

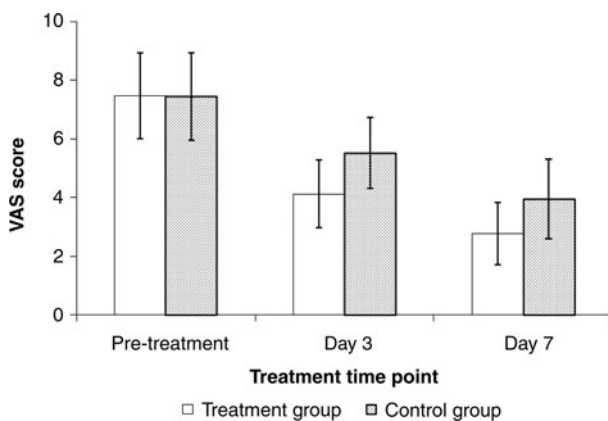


FIG. 2

VAS scores for subjective health state, for treatment and control groups, before and during treatment.

TABLE IV
SF36 QOL SCORES PRE- AND POST-TREATMENT

Time point	Score
<i>Treatment group</i>	
Pre-treatment	106.99 ± 6.64
Post-treatment	110.60 ± 6.14
<i>Control group</i>	
Pre-treatment	104.84 ± 6.60
Post-treatment	108.72 ± 6.04

Data represent means ± standard deviations. SF36 = Short Form 36 Health Questionnaire; QoL = quality of life

on the third day of treatment ($p = 0.004$) but no significant difference on the seventh day of treatment ($p = 0.937$) (Figure 4). Mild taste disturbance and mild to moderate oral mucosal numbness were the most frequent side effects, being reported by 28 of the 72 patients in the treatment group.

Sixteen patients did not complete the trial, and eight patients were excluded from the study in the follow-up period. A telephone survey of the 16 patients not completing the trial revealed various reasons for noncompletion: 14 stated that they could not get time off work to attend their follow-up appointment, while two stated that they were too ill to continue with the

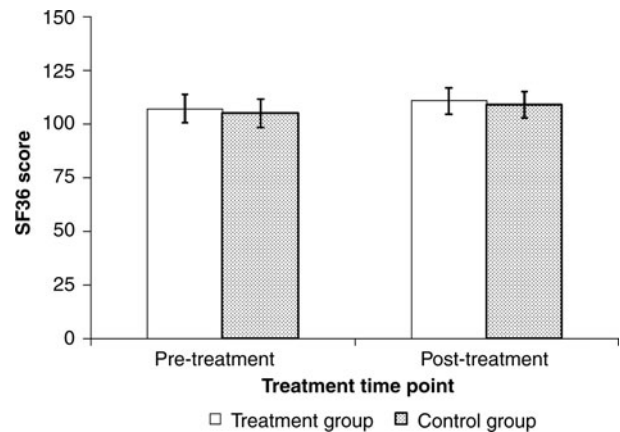


FIG. 3

Short Form 36 Health Questionnaire (SF36) scores for quality of life, for treatment and control groups, pre- and post-treatment.

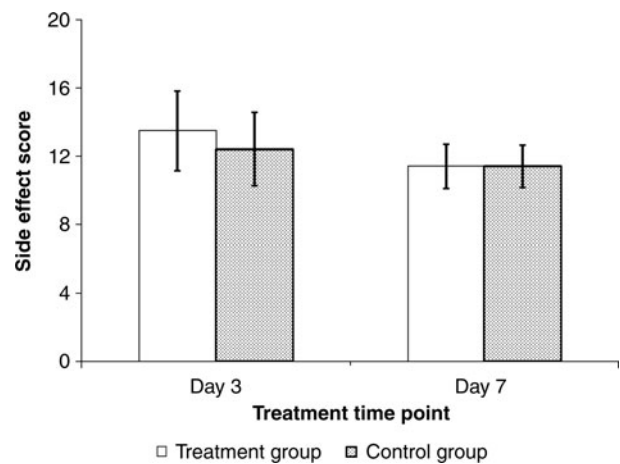


FIG. 4

Side effect scores for treatment and control groups on the third and seventh days of treatment.

trial. Eight patients were excluded from the study in the follow-up period due to other reasons.

Discussion

The aetiology of exudative pharyngitis is usually infectious: 40–60 per cent of cases are of viral origin and 5–40 per cent of bacterial origin.^{3,9} However, the combination of symptoms and clinical signs is usually inadequate to differentiate with certainty between viral and bacterial aetiology. For this reason, several different authorities (including the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the American Heart Association, the American Academy of Pediatrics, and the Infectious Diseases Society of America) have recommended that a diagnosis of streptococcal sore throat, in patients suspected for clinical and epidemiological reasons, should be confirmed by microbiological testing.^{10–14}

Although throat swab culture is the 'gold standard' for tonsillopharyngitis diagnosis, results are not available for 24–48 hours. An alternative is supplied by

the rapid antigen detection test, a quick and reliable test used in the diagnosis of group A streptococcal tonsillopharyngitis. Spadetto *et al.* assessed the reliability and validity of a rapid test for the identification of *S pyogenes* in pharyngeal exudate (a test similar to that used in the present study), in 430 patients presenting with tonsillopharyngitis; the test sensitivity was 91.2 per cent (negative predictive value = 96.5 per cent) and the test specificity 96.2 per cent (positive predictive value = 90.4 per cent).¹⁴ In our study, the rapid antigen detection test was used to diagnose patients with group A β -haemolytic streptococcal pharyngitis.

In cases of tonsillopharyngitis associated with group A β -haemolytic streptococcus, the limited evidence available suggests that a 10-day antibiotic course may reduce the number and frequency of attacks.³ Once group A streptococcal tonsillopharyngitis is diagnosed, either by throat culture or rapid testing, penicillin V is the first choice of treatment. The efficacy of this antibiotic has been demonstrated by many clinical studies. A 10-day penicillin course (given twice daily) is as efficacious as more frequent dosing regimens in the treatment of streptococcal tonsillopharyngitis.¹⁵ Hence, our study used penicillin V to treat patients with group A β -haemolytic streptococcal pharyngitis. However, while penicillin V is generally effective in the eradication of group A β -haemolytic streptococcus, it is not effective in reducing the associated pain. Thus, the main objectives of supportive treatment are to reduce tonsillopharyngeal inflammation and thus reduce pain, while also improving oral intake to avoid dehydration (and possible hospitalisation).⁹

At present, numerous pharmaceutical preparations (containing disinfectants, anti-inflammatory agents and/or topical anaesthetics) have been approved for the local treatment of acute pharyngitis.³ Our study assessed the effect of a mouth spray containing chlorhexidine gluconate and benzydamine hydrochloride.¹⁶ Benzydamine hydrochloride is an effective anti-inflammatory agent, while chlorhexidine gluconate is an antimicrobial agent frequently used for topical antiseptic effects. The effectiveness of chlorhexidine against gingivitis and recurrent oral mucosa ulceration has been shown in many studies.^{17,18} Chlorhexidine is effective against a wide variety of bacteria, including Gram-positives, Gram-negatives, aerobes and anaerobes.¹⁹ Chlorhexidine is effective against bacteria commonly found in the oral cavity, and against organisms associated with oral cavity disease.^{20–22} In addition to its *in vitro* antibacterial activity, studies have shown that chlorhexidine mouth rinse reduces the number of oral bacteria.^{23,24}

The present prospective, randomised, double-blinded, placebo-controlled study investigated the effect of chlorhexidine gluconate and benzydamine hydrochloride mouth spray, compared with placebo. The active treatment mouth spray was found to significantly reduce the intensity of clinical signs, without any evident side effects. The active treatment mouth spray

was also associated with improved quality of life over time, compared with placebo, although this improvement was not statistically significant.

Chlorhexidine gluconate is reported to have infrequent side effects, including tooth discolouration, taste disturbance and oral mucosa desquamation.²⁵ In our treatment group, those patients who reported side effects noted some taste disturbance or oral mucosa numbness for a few days following treatment. In our control group, no statistically significant side effects were observed on either the third or seventh day. The chlorhexidine–benzydamine mouth spray was generally very well tolerated, at the dosage administered, and no serious adverse events were observed.

- **Chlorhexidine gluconate and benzydamine hydrochloride mouth spray, added to standard antibiotic treatment, significantly alleviates the intensity of clinical signs in patients with streptococcal pharyngitis, compared with placebo**
- **Further research is necessary to fully assess the efficacy of this treatment in combating group A streptococcal tonsillopharyngitis**

It is possible that chlorhexidine–benzydamine mouth spray may be appropriate for patients who are unable to tolerate nonsteroidal anti-inflammatory drugs or steroids. Although this question was not addressed by the present study, chlorhexidine–benzydamine mouth spray may represent a safer and less costly form of analgesia for such patients, compared with current treatment options.

The present study had certain limitations. The power of the study was limited by its short duration (six months) and modest number of participants. Further research may be necessary to fully assess the efficacy of chlorhexidine–benzydamine mouth spray in treating group A streptococcal tonsillopharyngitis, using larger sample sizes or alternative control groups.

Conclusion

Chlorhexidine gluconate and benzydamine hydrochloride mouth spray, used in conjunction with standard antibiotic treatment, significantly decreases the intensity of clinical signs in patients with streptococcal pharyngitis.

References

- 1 Melio FR, Holmes DK. Upper respiratory tract infections. In: Rosen P, Barkin R. *Emergency Medicine: Concepts and Clinical Practice*, 4th edn. St Louis: Mosby, 1998;1529–53
- 2 Shores CG. Infections and disorders of the neck and upper airway. In: Tintinalli JE, Kelen GD, Stapczynski JS. *Emergency Medicine: a Comprehensive Study Guide*, 6th edn. New York: McGraw-Hill, 2004;1494–501
- 3 Scottish Intercollegiate Guidelines Network. *Management of Sore Throat and Indications for Tonsillectomy*. Guideline No: 117 April 2010 (<http://www.sign.ac.uk/guidelines/fulltext/117/index.html>)
- 4 Del Mar CB, Glasziou PP, Spinks AB. Antibiotics for sore throat. *Cochrane Database Syst Rev* 2006;(4):CD000023

- 5 National Institute for Health and Clinical Excellence. *NICE Guideline. Respiratory tract infections – antibiotic prescribing. Prescribing of antibiotics for self-limiting respiratory tract infections in adults and children in primary care*. In: <http://www.nice.org.uk/nicemedia/pdf/CG69FullGuideline.pdf> [16.01.2001]
- 6 Wewers ME, Lowe NK. A critical review of visual analogue scales in the measurement of clinical phenomena. *Research in Nursing and Health* 1990;**13**:227–36
- 7 Diaz-Buxo JA, Lowrie EG, Lew NL, Zhang H, Lazarus JM. Quality-of-life evaluation using Short Form 36: comparison in hemodialysis and peritoneal dialysis patients. *Am J Kidney Dis* 2000;**35**:293–300
- 8 McHorney CA, Ware JE, Raczek AE. The MOS 36-item short form health survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Med Care* 1993;**31**:247–63
- 9 Wei JL, Kasperbauer JL, Weaver AL, Boggust AC. Efficacy of single-dose dexamethasone as adjuvant therapy for acute pharyngitis. *Laryngoscope* 2002;**112**:87–93
- 10 Bisno AL, Gerber MA, Gwaltney JM, Kaplan EL, Schwartz RH, Infectious Diseases Society of America. Practice guidelines for the diagnosis and management of group A streptococcal pharyngitis. Infectious Diseases Society of America. *Clin Infect Dis* 2000;**35**:113–25
- 11 Ebell MH. Making decisions at the point of care: sore throat. *Fam Pract Manag* 2003;**10**:68–9
- 12 Dajani A, Taubert K, Ferrieri P. Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the American Heart Association. Treatment of acute streptococcal pharyngitis and prevention of rheumatic fever: a statement for health professionals. *Pediatrics* 1995;**96**:758–64
- 13 American Academy of Pediatrics. Committee on Infectious Diseases. American Academy of Pediatrics. Committee on Infectious Diseases. Severe invasive group A streptococcal infections: a subject review. *Pediatrics* 1998;**101**:136–40
- 14 Spadetto CC, Camara SM, Ingles MJA, Escuret JM, Barcelo IC, Sanchez FR. Rational use of antibiotics in pediatrics: impact of a rapid test for detection of beta-haemolytic group A streptococci in acute pharyngotonsillitis [in Spanish]. *An Esp Pediatr* 2000;**52**:212–19
- 15 Efstratiou A. Group A streptococci in the 1990s. *Antimicrob Chemother* 2000;**45**Suppl:3–12
- 16 Matthijs S, Adriaens PA. Chlorhexidine varnishes: a review. *J Clin Periodontol* 2002;**29**:1–8
- 17 Killoy WJ. The use of local-delivered chlorhexidine in the treatment of periodontitis. Clinical results. *J Clin Periodontol* 1988;**25**:953–8
- 18 Burgess JA, Johnson BD, Sommers E. Pharmacological management of recurrent oral mucosal ulceration. *Drugs* 1990;**39**:54–65
- 19 Emilson CG. Susceptibility of various microorganisms to chlorhexidine. *Scand J Dent Res* 1977;**85**:255–65
- 20 Hennessey TD. Antibacterial properties of Hibitane. *J Clin Periodontol* 1977;**4**:36–48
- 21 Newman MG, Hulem C, Colgate J, Anselmo C. Antimicrobial susceptibility of plaque bacteria. *J Dent Res* 1979;**58**:1722–32
- 22 Hesselgren SG, Dahl GM, Larje O. In vitro experiments with chlorhexidine on pure bacterial and fungal cultures from the mouth. *Swed Dent J* 1971;**64**:801–6
- 23 Briner WW, Grossman E, Buckner RY, Rebitski GF, Sox TE, Setser RE *et al*. Effect of chlorhexidine gluconate mouth rinse on plaque bacteria. *J Periodont Res* 1986;**21**(suppl 6):44–52
- 24 Ferretti GA, Ash RC, Brown AT, Largent BM, Kaplan A, Lillich TT. Chlorhexidine for prophylaxis against oral infections and associated complications in patients receiving bone marrow transplants. *J Am Dent Assoc* 1987;**114**:461–7
- 25 Field EA, Allan RB. Review article: oral ulceration aetiopathogenesis, clinical diagnosis and management in the gastrointestinal clinic. *Aliment Pharmacol Ther* 2003;**18**:949–62

Address for correspondence:

Dr Ahmet Ural,
Karadeniz Teknik Üniversitesi Tıp Fakültesi Farabi Hastanesi,
Kulak Burun Boğaz Hastalıkları Anabilim Dalı,
61080 Trabzon, Turkey

Fax: +904623250518

E-mail: ahmetural2001@yahoo.com

Dr A Ural takes responsibility for the integrity of the content of the paper
Competing interests: None declared

APPENDIX I

GUIDELINES FOR ASSESSING THE INTENSITY OF CLINICAL SIGNS OF GROUP A β -HAEMOLYTIC STREPTOCOCCAL TONSILLOPHARYNGITIS

Clinical sign	Mild	Moderate	Severe
Sore throat	Some discomfort upon swallowing, pain easily tolerated	Pain intermittently present whether swallowing or not; difficulty swallowing	Continuous pain whether swallowing or not; swallowing very difficult
Erythema of posterior pharynx	Distinct but slight redness limited to single anatomical structure of posterior pharynx	Between that described for 'mild' & 'severe', or redness involving 2 or 3 anatomically distinct structures of posterior pharynx	Intense, bright, deep, 'fiery', 'beefy' or marked redness involving 2 or more anatomical structures of posterior pharynx, or 'moderate' redness involving >75% of posterior pharyngeal structures
Oedema of posterior pharynx	Minimal but distinct swelling limited to single anatomical structure of posterior pharynx	Between that described for 'mild' & 'severe', involving 1–3 anatomically distinct posterior pharyngeal structures	Marked swelling of 1 or more anatomically distinct posterior pharyngeal structures, including 'kissing' or near-kissing tonsils & swelling extending onto soft palate or buccal area; or 'moderate' swelling involving >75% of posterior pharyngeal structures
Exudate	1 or 2 punctate (<2 mm) areas of exudate	1 or more distinct areas of exudate, at least 1 of which is 2 mm in size	Confluent exudates covering >50% of posterior pharyngeal structures; or exudates completely covering 1 or both tonsils or posterior pharynx
Cervical lymphadenopathy	1–2 cm, non-tender	1–3 cm, tender	>3 cm, tender
Headache	Discomfort tolerated without analgesia	Requires & responds to non-narcotic analgesia	Requires & responds to narcotic analgesia, or responds poorly and inadequately to non-narcotic analgesia