

Adjuvant prednisone therapy in pharyngitis: a randomised controlled trial from general practice

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ABSTRACT

Background

Acute pharyngitis is a frequent and well-documented complaint in general practice but the associated suffering has remained largely unaddressed in the literature. Evidence, however, from five randomised controlled trials suggests that corticosteroids may be useful in relieving pain and discomfort arising from the condition.

Aim

To determine if short-acting oral therapy with prednisone was more effective than placebo in alleviating the suffering from acute pharyngitis in adults in a general practice setting.

Design of study

Randomised placebo-controlled trial.

Setting

General practice in Israel.

Method

Patients with acute pharyngitis were randomised to receive 60 mg prednisone orally for 1 or 2 days, or identical placebo treatment. The main outcome measures were throat pain, measured by a visual analogue scale at 12, 24, 48 and 72 hours after presentation, time off work, fever, dysphagia, recurrence of symptoms and bacterial recurrence.

Results

Patients treated with prednisone experienced more rapid throat pain resolution than those in the placebo group. No adverse effects were reported nor any differences between the two groups regarding either symptom or positive bacterial culture recurrence.

Conclusion

Short-acting oral steroid therapy is effective for shortening throat pain duration in acute pharyngitis.

Keywords

corticosteroids; pharyngitis; placebos; randomised controlled trials.

INTRODUCTION

Acute infectious inflammation of the throat is a frequent reason for medical consultations in all age groups.¹ Although generally mild in nature, it may give rise to significant suffering and morbidity, including throat pain, pain on swallowing, trismus, high fever, difficulty in eating and drinking, and the need for time off work or school. Antibiotic therapy may shorten the duration of the disease and prevent some of its potentially severe consequences.² However, symptom relief remains largely unaddressed in the literature, and is frequently only allocated some general remarks about the judicious use of analgesics and antipyretics while awaiting spontaneous resolution.

Corticosteroids are powerful anti-inflammatory agents whose short-term use in diminishing inflammation in asthma, bronchiolitis,³ croup,⁴ acute allergic reactions and inflammatory joint disease is well documented as being both safe and effective. Five randomised control trials have reported the use of adjuvant corticosteroid treatment in acute pharyngitis among hospital emergency room patients.⁵⁻⁹ In these studies, steroid treatment was found to be beneficial in reducing both the duration and intensity of pain and discomfort.

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Submitted: 22 September 2003; **Editor's response:** 10 March 2004; **final acceptance:** 27 July 2004.

©British Journal of General Practice 2005; 55: 218-221.

The aim of this study was to measure the effect of short-term oral prednisone adjuvant therapy on symptoms of acute pharyngitis in general practice patients, and to compare this effect in patients with an initially positive or negative throat culture.

METHOD

The study was conducted by five GPs in three urban and one rural Israeli family medicine clinics between November 2001 and October 2002. All 18–65-year old patients presenting with a severe sore throat and at least two out of four additional criteria (tonsillar/pharyngeal exudate, dysphagia, fever, lymphadenopathy) were invited to take part in the study. The potential benefits and risks of short-term oral steroid therapy were explained to all patients, and those consenting to participate in the study signed a detailed consent form. Only one patient out of the 80 patients eligible to take part refused to enter the study. Pregnant women, patients already on steroid therapy or with a malignant disease, diabetes, immunodeficiency or tonsillar abscess, and those unable to give informed consent were excluded.

A table of random numbers was generated using an electronic spreadsheet, and the numbers in the table were used to prepare treatment packages. Recruited subjects were randomly assigned to either the study or placebo arm of the investigation by chance selection of the treatment package. These packages contained envelopes with either the active drug or the placebo tablets (identical to the active tablets), data collection sheets, and visual analogue scales (VAS). Both patients and doctors were blinded to the treatment given. Each subject was then examined clinically, had a throat swab taken, and was given a VAS and either 60 mg prednisone orally (three 20 mg tablets) or three identical placebo tablets from their treatment pack. Antibiotic treatment (penicillin VK, amoxicillin or erythromycin) was prescribed at the GPs' discretion but was ceased if the throat culture subsequently proved negative for Group A streptococci. The use of non-prescription pain medication by patients was permitted but was not controlled. A second similar dose of oral steroid or placebo was taken the following

day. After 40 patients had been recruited, this second dose was waived in order to compare the effects of 1-day and 2-day prednisone treatment.

Initially, all patients were asked to rate their pain on a 10 cm numbered VAS where 0 represented no pain and 10 the worst pain the patient had ever experienced. Each patient was asked about throat pain, pain on swallowing, fever, and the need for time off work or studies due to their illness. They were asked again during four telephone follow-ups by their own GP at 8–12, 24, 48 hours and 7 days after study entry. Pain and discomfort were also sequentially reassessed using the initial VAS instrument, which patients were instructed to use at home. Finally, 2 weeks after study entry the subjects were questioned about any symptom recurrence, and a second throat swab was taken if the initial one had been positive.

Data handling and statistical analysis

The information collected from each patient was recorded on a data sheet and computerised for analysis using Epi-Info Version 6 software (Centers for Disease Control, Atlanta, GA). Student's *t*-test was employed to compare means of pain scores and the χ^2 statistic to compare proportions of patients with other symptoms. Significance was set at the 5% level. The sample size calculation was performed using the method of Dupont and Plummer.¹⁰ A predicted 50% reduction in the pain score or proportions of other outcome variables would require at least 18 patients in each arm of the trial.

RESULTS

Enrollment

Eighty patients were initially recruited into the study; one refused to participate after receiving details of the investigation. Written informed consent was obtained from the remaining 79 participants (50 women and 29 men with a mean age of 34 years) of whom 40 were randomised to the prednisone arm and 39 to the placebo arm. The flow of participants through each stage of the trial is depicted in the CONSORT diagram (Figure 1).

Baseline characteristics

At enrollment, patients in both study groups were similar regarding sociodemographic characteristics, disease severity (Table 1), VAS pain scores, presence or absence of fever, exudate, dysphagia and lymphadenopathy. No differences were noted in patient characteristics among the referring GPs.

Follow-ups

Complete follow-up data at 12, 24, 48 and 72 hours were obtained from all patients (Table 2). The mean

How this fits in

Therapy with long-acting injected corticosteroids has been shown to speed symptom relief in patients presenting to emergency departments with acute pharyngitis. This study demonstrates the efficacy of short-acting oral therapy with prednisone in relief of pain in patients with acute pharyngitis in the general practice setting.

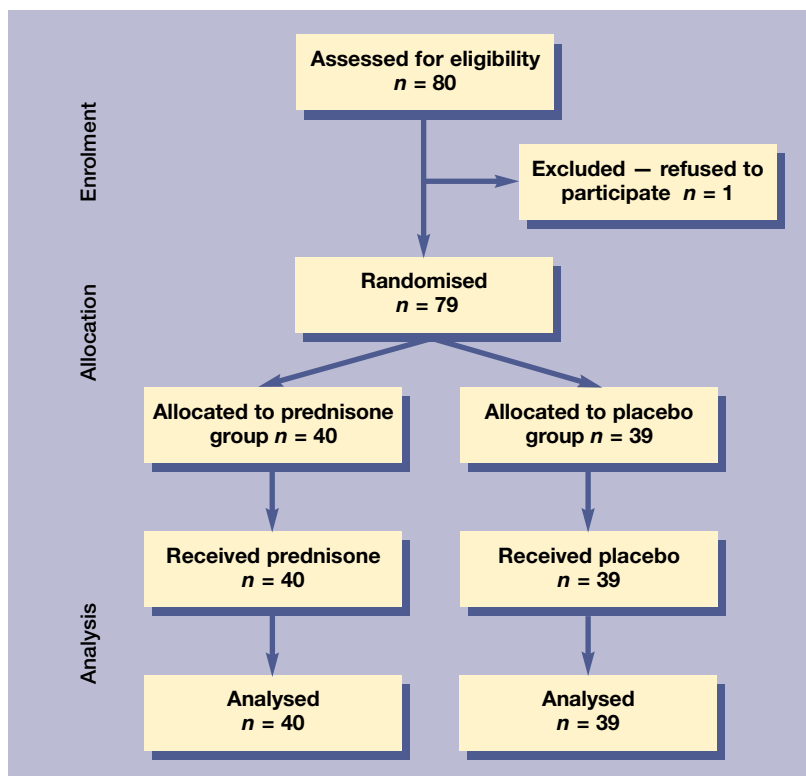


Figure 1. CONSORT diagram showing the flow of participants through each stage of the trial.

VAS pain score was significantly lower in the prednisone group at the 12- and 24-hours follow-up. The percentage fall in the pain score was also significantly greater in the prednisone group at these times. By 36 hours the difference in the mean VAS score between the two groups was no longer significant, nor at 72 hours. The time to all pain disappearance was significantly shorter in the prednisone group, among whom 57% were pain free at 48 hours compared with only 33% in the placebo group at the same time. No significant differences in time taken off work or studies were recorded between the two groups at any follow-up period.

Table 1. Initial study population characteristics.

	Prednisone n = 40	Placebo n = 39
Mean age in years (SD)	32.4 (9.1)	35.4 (11.5)
Female (%)	72.5	53.8
Patients with throat pain (%)	40 (100)	39 (100)
Patients with fever (%)	24 (60)	25 (64)
Patients with exudate (%)	35 (87)	34 (87)
Patients with lymphadenopathy (%)	36 (90)	35 (89)
Patients with dysphagia (%)	39 (97)	39 (100)
Mean pain score VAS (SD)	8.0 (1.6)	7.4 (1.8)
Patients requiring time off work (%)	22 (55)	27 (69)
Patients with streptococcal infection (%)	18/35 (51)	24/38 (63)

SD = standard deviation. VAS = visual analogue scale.

Bacterial pathogens

Results of initial throat swab culture were obtained for 73 (92%) patients. The 42 (57%) swabs found positive for Group A β -hemolytic streptococci were distributed equally between both study groups and all patients subsequently received antibiotic therapy. All 42 were invited to re-attend for a follow-up throat swab 2 weeks later, and 32 (80%) did return. Of these, 13 belonged to the prednisone group and 19 to the placebo group. There was no significant difference in the presence of streptococci in these follow-up throat swabs between the two groups (2/13 in the prednisone group versus 3/19 in the placebo group). Stratified analysis revealed that patients with cultures initially positive for streptococcus who received prednisone had significantly lower pain scores after 12 and 24 hours compared with similar patients who received placebo. For patients with initially negative cultures, the effect of prednisone on reducing VAS pain scores was only significant after 12 hours and was not apparent at any subsequent follow-up.

Recurrence of symptoms

Six patients reported a recurrence of symptoms at the final 2-week follow-up, one in the prednisone group and 5 in the placebo group (not statistically significant). The time to recurrence of symptoms was not significantly different between the two groups.

Dose effect

A significant dose effect was found between the 1-day and 2-day treatment prednisone schedules. A comparison of VAS rated pain scores in the 2-day treatment group revealed significantly lower pain scores in the prednisone group, compared with the placebo group, at the 12-, 24- and 48-hour follow-ups. However, no similar VAS score differences between the groups were detected at any follow-up period for participants who received only a single dose of prednisone.

DISCUSSION

Summary of the main findings

As far as we are aware, this study is the first report on the effective use of short-acting oral steroids in painful pharyngitis and similarly the first to have been performed entirely in primary care using simple inclusion criteria. It is, therefore, a useful addition to the growing body of knowledge about the value of steroids in relieving suffering from acute infection in different settings. The symptom relief reported by patients in this study would appear to justify the use of steroids in patients with severe pharyngitis in spite of the small risks of this therapy; risks that also exist with non-steroidal analgesic therapy. No increase in bacteriological or clinical recurrence was found among the patients treated with

steroids although such a possibility is sometimes put forward as a reason for shunning steroids in acute infection. Similarly, no adverse effects were observed from this short-term steroid therapy. However, this study was small and lacked the power to detect serious but rare adverse effects of therapy. Risks of severe side effects are related to long-term, high-dose steroid therapy. Rare adverse effects such as avascular necrosis of the femoral head or complications due to increased viral replication are possible, but unlikely from single dose therapy.

Strengths and limitations of this study

We were unable to demonstrate the value of a single dose of prednisone for symptom relief compared with a 2-day schedule, but this may have been due to insufficient study power as only a small sub-group could be used in this analysis. Although the study did not control for analgesic use, there is no reason to believe that the patterns of such use were different in the two groups, which were not significantly different regarding clinical and demographic characteristics on enrollment. The high rate of swabs found to be positive for streptococcus in this study is noteworthy, and may be due to the inclusion criteria that favoured the recruitment of more seriously ill patients.

Comparison with existing literature

Five previous investigations that employed a VAS for pain measurement (and included adolescent as well as older patients) have already demonstrated the benefit of steroids in reducing suffering in acute pharyngitis. However, as these were all conducted in hospital outpatient or emergency department setting, they may have included patients with more severe symptoms. Also, they all relied on the use of a long-acting injectable steroid in at least one arm of the trial. The mechanism of action of steroids for symptom relief in such circumstances is still not entirely clear but may be related to its anti-inflammatory effect, that is, decreasing pharyngeal oedema. This is consistent with findings from surgical studies using injection of steroids in the tonsillar bed to reduce pain following tonsillectomy.¹¹ The study by Bulloch *et al* found little benefit for symptom relief from treatment of pharyngitis with dexamethasone in children.⁹ They did find a statistically significant advantage in those patients with evidence of streptococcal infection, although the clinical value was marginal.

Implications for future research and clinical practice

Overall, this study has shown that short-acting adjuvant oral steroid therapy appears to be safe and more effective than placebo for symptom relief in adults with severe acute pharyngitis presenting in general practice.

Table 2. Outcome measures comparing patients treated with prednisone and placebo.

	Prednisone <i>n</i> = 40	Placebo <i>n</i> = 39	<i>P</i> -value	Difference of means	95% CI
Mean (SD) throat pain score					
VAS at 12 hours	3.9 (2.5)	5.9 (2.3)	<0.001	-2.02	-0.9 to -3.35
VAS at 24 hours	2.4 (2.6)	4.5 (2.9)	0.002	-2.1	-0.77 to -3.22
VAS at 48 hours	1.8 (2.5)	2.6 (2.6)	0.13	-0.8	-0.04 to 2.04
VAS at 72 hours	1.2 (2.3)	1.2 (1.7)	0.9	0	-1.2 to 1.1
Proportion of patients pain free (%)					
				OR	
at 12 hours	27.5	2.6	0.006	0.07	0.0 to 0.58
at 24 hours	42.5	10.3	0.003	0.15	0.04 to 0.58
at 48 hours	57.5	33.3	0.053	0.37	0.13 to 1.02
at 72 hours	72.5	53.8	0.13	0.44	0.15 to 1.26
Proportion of patients with recurrence at 2-week follow-up (%)	2.6	13.2	0.12	0.18	0.01 to 1.75

OR = odds ratio. SD = standard deviation. VAS = visual analogue scale.

Ethics committee and reference number

The Ethics Committee for Research on Human Subjects of the Rabin Medical Center, Petach Tikva, Israel, (2414)

Competing interests

None

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