Short course of systemic corticosteroids in sinonasal polyposis: A double-blind, randomized, placebo-controlled trial with evaluation of outcome measures

Pravin Hissaria, DM,[a] William Smith, PhD,[b] Peter J. Wormald, MD,[c] James Taylor, FRANZCR,[d] Mathew Vadas, PhD,[a] David Gillis, FRCPA,[a] and Frank Kette, PhD[b]

Adelaide, Australia

Background: Topical and systemic corticosteroids are the first choice in medical treatments for sinonasal polyposis, but surprisingly, there is no high-level evidence for the efficacy of oral corticosteroids.

Objective: The aim of this study was to establish the efficacy of a short course of oral prednisolone in ameliorating the symptoms of sinonasal polyposis, as well as reducing mucosal inflammation assessed by means of nasendoscopy and magnetic resonance imaging (MRI). A secondary aim was to evaluate the relationship between outcome measures.

Methods: Subjects with symptomatic endoscopically diagnosed sinonasal polyposis received 50 mg of prednisolone daily for 14 days or placebo. Outcome was quantified by using the modified 31-item Rhinosinusitis Outcome Measure questionnaire, physician's assessment, nasendoscopy with photography, and MRI.

Results: There were 20 subjects in each treatment group. Only the prednisolone-treated group showed significant improvement in nasal symptoms ($P < .001$). The Rhinosinusitis Outcome Measure score improved in both groups, but the prednisolone-treated group had significantly greater improvement than the placebo group ($P < .001$). Objectively, there was significant reduction in polyp size, as noted with nasendoscopy ($P < .001$) and MRI ($P < .001$), only in the prednisolone-treated group. The outcome measures correlated with each other; the highest level of correlation was between the objective measures of nasendoscopy and MRI ($R^2 = 0.76$, $P < .001$). There were no significant adverse events.

Conclusion: This trial clearly establishes clinically significant improvement in the symptoms and pathology of sinonasal polyposis with a short course of systemic corticosteroids. MRI scanning and quantitative nasendoscopic photography are objective and valid tools for assessing the outcome of treatment in this condition.

Clinical implications: A 14-day course of 50 mg of prednisolone is safe and effective therapy for symptomatic nasal polyposis.

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Key words: *Nasal polyps, corticosteroids, medical treatment, 31-item rhinosinusitis outcome measure, endoscopy, magnetic resonance imaging, outcome, randomized, double blind, placebo controlled*

Sinonasal polyposis is a chronic disorder with a major effect on the quality of life of affected individuals. The management options for sinonasal polyposis are medical treatment, surgery, or a combined approach. It is a common practice to use systemic or topical corticosteroids as the first therapeutic choice, followed by surgery for resistant or recurrent cases. There is good evidence, in the form of randomized controlled trials, to support the use of topical nasal corticosteroids.[1,2] Short courses of systemic corticosteroids are also widely used in clinical practice to provide rapid relief of symptoms, followed by the use of long-term topical corticosteroids.[3,4] The efficacy of systemic corticosteroids is well reported; there is usually a dramatic reduction in symptoms, and it has been termed a *medical polypectomy*. However, it is surprising to note that there have been no published randomized placebo-controlled trials of systemic corticosteroids to confirm their efficacy on the symptoms and pathology of sinonasal polyposis.[5]

Various outcome measures have been used to analyze the results of intervention in this patient population.[6,7] Most of these are questionnaire-based visual analogue scores of symptoms and quality of life. Intranasal polyps can be visualized by means of nasendoscopy, and sinonasal polyp tissue can be shown by using imaging methods, such as computed tomography (CT) and magnetic resonance imaging (MRI); these approaches offer more objective methods of measuring treatment response. Many previous studies have shown a poor relationship between symptoms and objective measurements of pathology.[8-10] In this article we describe a randomized,

From [a]the Department of Human Immunology, Institute of Medical and Veterinary Sciences; the Departments of [b]Immunology and Allergy and [d]Radiology, Royal Adelaide Hospital; and [c]the Department of Surgery–Otorhinolaryngology Head & Neck Surgery, Universities of Adelaide and Flinders.

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Reprint requests: William Smith, PhD, Clinical Immunology and Allergy, Ward R8, Royal Adelaide Hospital, North Terrace, Adelaide, South Australia 5000. E-mail: wsmith@mail.rah.sa.gov.au.

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Abbreviations used
CT: Computed tomography
MRI: Magnetic resonance imaging
RSOM-31: Thirty-one–item rhinosinusitis outcome measure

double-blind, placebo-controlled trial of a short course of systemic corticosteroids, using as outcome measures the physician history, a patient questionnaire (the 31-item Rhinosinusitis Outcome Measure [RSOM-31]), MRI of the paranasal sinuses, and nasendoscopy. We have used a novel but simple method of nasendoscopic quantification of nasal polyp size, validated it against the other outcomes, and assessed the correlation between these measures.

METHODS

Patients

Forty-one subjects aged 18 to 65 years drawn mainly from allergy outpatient clinics who had symptomatic polyp disease diagnosed on nasendoscopy were included in the study. Exclusion criteria included previous use of oral steroids, unstable asthma, recent sinus surgery, acute infection within 1 month of recruitment, polyps caused by cystic fibrosis or mucociliary disorders, diabetes mellitus, cataract, glaucoma, fungal sinusitis, contraindications for MRI scanning, or any other significant comorbid condition that contraindicated the use of systemic corticosteroids. Subjects were allowed to continue the use of regular antihistamines, topical corticosteroids, or both. These patients were randomized by the hospital pharmacy to receive the study medication, which consisted of 50 mg of prednisolone or placebo daily for 14 days, and were blinded to their treatment status. This dose was selected as the maximum safe dose in adults that could be given for 14 days without inducing lasting adrenal suppression, thus allowing drug cessation without tapering.[11] Immediately on completion of the study investigations, the subjects were unblinded by an independent physician (study personnel were not informed of the patient's treatment status until all assessments were completed) and offered open treatment; all who had taken placebo were offered and accepted a course of prednisolone. Therefore in this study we did not undertake long-term follow-up of the subjects because all of them ultimately received prednisolone. The study was approved by the Medical Ethics Committee of the Royal Adelaide Hospital.

Physician assessment

Baseline assessment included full history; physical examination; ear, nose, and throat examination; skin prick testing; pregnancy testing (in female subjects of childbearing age); and blood glucose level measurement. Physician assessment at both entry and exit visits included grading nasal symptoms (6 scales: congestion, hyposmia, rhinorrhea, sneezing, postnasal drip, and itch) and other related symptoms (4 scales each for eyes and ears and 2 scales for general well-being) on a visual analog scale of 1 to 5 (mild to severe) based on the patient history. Adverse symptoms were recorded at visit 2, and subjects were also asked about symptoms after cessation of the study drug on subsequent follow-up.

RSOM questionnaire

The RSOM-31 questionnaire[6] assesses 6 nasal symptoms (congestion, rhinorrhea, sneezing, hyposmia, postnasal discharge, and thick nasal debris) and 25 other symptoms in several domains (ocular, ear, sleep, general symptoms, practical problems, and emotional consequences) by using a visual analog scale score of 1 to 5 for symptom severity and 1 to 5 for symptom importance. Patients were asked to fill out the questionnaire at baseline and after 2 weeks of therapy, without assistance from the medical personnel. We used a modification of this questionnaire; subjects had difficulty understanding the importance parameter, and therefore we used severity scores only. We note that in a subsequent development of the RSOM-31 by the group that developed it, the 20-item Sinonasal Outcome Test score,[7] the importance parameter was relinquished. We did not use the Sinonasal Outcome Test because it omits questions on nasal congestion and anosmia, cardinal features of polyposis.

MRI of the paranasal sinuses

MRI of the paranasal sinuses was done immediately before and after 2 weeks of prednisolone treatment. T1 and T2 scans were scored by 2 experienced observers who were blind to treatment status. Pretreatment and posttreatment scans were scored independently according to defined criteria; each sinus group (maxillary, ethmoid, frontal, and sphenoid), right and left, and the nasal cavity itself was scored as follows, which produced a theoretic maximum score of 40: score 0, normal—mucosa of less than 1 mm and no polyp; score 1, mild—mucosa of 1 to 3 mm and a polyp of less than 6 mm; score 2, moderate—mucosa of 3 to 6 mm and a polyp of 6 to 12 mm; score 3, severe—mucosa of greater than 6 mm and a polyp of greater than 12 mm; and score 4, obliterated—sinus/nasal cavity filled with polyp/mucosa.

Nasendoscopy

Nasendoscopy was carried out immediately before commencement of prednisolone treatment and after 2 weeks of treatment by using an Olympus rigid telescope (30°, 4 mm; A7595A; Tokyo, Japan) with a 300-W Xenon light source (CLV-S30), a video adapter 1.2× (AR-SX12E), a camera control unit (OTV-SX2C), and a triple-chip camera head (MAJ-387N). Images were recorded with a Sony Digital Still Image Capture Adaptor (MVC-FDR3E; Tokyo, Japan). To document the position at which images were captured, the nasendoscope was calibrated in centimeters with an indelible marker, and the distance of passage of the endoscope past the nasal tip in centimeters, as well as the angle (superior, middle, and inferior), was recorded. After treatment, repeat photographs were taken by using the same distance/angle measurements to reproduce the original field of view as closely as possible. For scoring, we compared pretreatment and posttreatment groups of images paired for each study subject according to comparable fields of view. The photographs were viewed on the computer screen; observers were blind to active/placebo treatment status and to pretreatment/posttreatment order. Observers selected the group of images showing the more extensive/larger polyps and estimated the percentage reduction in polyp size in the other group. The results from the assessment of 4 clinicians (3 immunologists and 1 ear, nose, and throat surgeon) were pooled for analysis. The intraclass correlation analysis showed a good measure of consistency among the 4 raters (0.96). The measure of absolute agreement among the raters was 0.57. The predicted reliability of these measurements using a mean of 3 replicate measurements resulted in a reliability of 0.80.[12] Grades were also assigned at the time of endoscopy according to the system of Lund and Mackay[13]; however, polyp grading was not suitable for evaluation of treatment because it is a qualitative scale.

Statistics

The χ^2 and Student t tests were used to determine the significant differences between the 2 treatment arms. Comparison between different outcome measures was done by using the Spearman correlation coefficient. Intraclass correlation analysis was estimated as part of an