Clinical Assessment of Disease Severity in Recurrent Aphthous Stomatitis

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Purpose: Recurrent aphthous stomatitis (RAS) is one of the most common oral mucosal diseases in many parts of the world. However, there is very limited published clinical evidence for the therapies used in this condition. This could be partly due to the difficulty in assessing the efficacy of treatment. In this paper, a method for assessing and monitoring the severity of ulcers after treatment in RAS is presented.

Materials and Methods: Six ulcer characteristics; number, size, duration, ulcer-free period, site and pain were used to generate an ulcer severity score. The score for 223 RAS patients, 79 of whom were scored again after three months therapy with topical betamethasone, were analysed.

Results: The scores for the minor RAS group were between 18-43 (mean 29.2 ±5.3). The mean score in the major RAS group (range: 28-60, mean 39.9 ±6.1) was significantly greater than in the minor group ($p<0.001$). The herpetiform RAS score range was wide (range: 18-57, mean 36.6 ±8.4). The mean severity score decreased significantly after treatment ($p<0.001$).

Conclusions: The ulcer severity score has been shown to be an aid in the management of patients with RAS. The severity of the disease is converted to numerical values therefore helping in assessing the efficacy of treatment. This method may well prove to be of value in research and in clinical trials.

Key words: stomatitis, aphthous, oral ulcers, disease management

Oral Biosci Med 2005; 2: 5-13 *Submitted for publication 5 November 2004; accepted for publication 9 December 2004*

INTRODUCTION

Recurrent aphthous stomatitis (RAS) is a distinct oral disease of unknown aetiology characterised by the spontaneous emergence of more than two bouts of oral ulcers per year, not knowingly associated with ulcers elsewhere in the body or with an underlying systemic abnormality. RAS is a common oral ulcerative disease in many parts around the world (Embil et al, 1975; Fahmy, 1976; Rennie et al, 1985; Pongissawaranun and Laohapand, 1991). It should be diagnosed after careful consideration of the patient's history, clinical appearance of the disease (Lehner et al, 1968) and the results of relevant investigations to avoid confusion with ulcers secondary to systemic disease (Rogers et al, 1997; Krause et al, 1999) and nutritional or haematological deficiencies (Challacombe et al, 1977, 1983; Wray et al, 1978; Field et al, 1987; Porter et al, 1988; Nolan et al, 1991).

One major impediment to the study of RAS has been the lack of a widely accepted measure of the disease severity, which could be applied to every patient diagnosed with this condition. In published RAS studies, the methods used for the assessment of RAS are usually individually designed to suit the aims of that particular study. Researchers have mostly used the patient's history (Sun et al, 1994), frequent clinical examinations (Merchant et al, 1978; Miller et al, 1980; Khandwala et al, 1997), patients' diaries (Wray et al, 1978; Hunter and Addy 1987; Taylor et al, 1993), and clinical photographs (Merchant 1978) to monitor healing and response to treatment. These methods are by and large suitable for research where the number of patients is confined within a certain time span. They are not generally considered practical for universal and routine clinical use. There is a general consensus that the development of guidelines for the quantification of oral mucosal disease is desirable, but that this whole field was underdeveloped to date (Flint et al, 2002).

In clinical trials RAS has usually been assessed by using a selection of the ulcer features recognised as part of the elementary history taking for the diagnosis of ulcers, which are; the average number in a crop, size, duration, frequency of the attacks, oral sites affected and pain. Most of the published studies have used two to three of these features to monitor the progress of the condition (Miller et al, 1978; Hunter and Addy, 1987; Taylor et al, 1993; Katz et al, 1994; Khandwala et al, 1997; Wray, 1978; Sun et al, 1994, Hunter et al, 1979; Linton and Melin, 1982). Only very few used a wider selection although there is no evidence in the literature that any one of these characteristics is a better marker for the severity and the progression of RAS than another; in fact clinical evidence suggests that all six are important for the diagnosis of RAS and have roughly an equal impact on the patient's quality of life. Methods using a wider range of the ulcer characteristics to assess the improvement in the condition are therefore likely to be more credible than others using one or two features of the ulcers only.

The aim of this paper is to present a method for the clinical assessment of disease severity in RAS that has proved to be easy to use and useful in the systematic management of patients in an oral medicine clinic.

MATERIALS AND METHODS

A full history of the patients was taken. For the purposes of scoring the severity of RAS, the characteristics of the ulcer attacks in the preceding three months were recorded on a form devised especially to ensure that the fundamental questions for assessing the ulcers are asked: average size of the ulcers, the number of ulcer within an attack, the duration of the ulcer, the frequency of the ulcer attacks, the sites affected and whether the ulcers are painful enough to interfere with routine life. A note of the medication taken for the ulcers and whether there is evidence for scarring was made (Fig 1). A separate form was completed on every visit for every patient diagnosed with RAS. The patient's description of the ulcers were verified clinically whenever possible. To facilitate the objective comparison of the severity of the condition especially before and after treatment, the ulcer characteristics were converted into numbers to give an ulcer severity score (USS).

The USS was developed with the premise that more than 95% of RAS episodes comprise ulcers that are: less than 20 in number, less than 20mm in diameter, lasts for less than five weeks and recur in less than 10 weeks. The calculation of the scores was as follows:

1. **Number:** the score corresponds to the average number of ulcers per crop; ie. a patient having on average four ulcers would score 4 for this parameter. The maximum for this parameter was set at 20 to accommodate for the ulcer attacks that have more than 10 but without giving undue weight for this parameter.
2. **Size:** The score corresponds to the average diameter of the ulcers in millimetres; ie. a patient having ulcers of average size of 5mm would score 5. Patients indicated the average size of their ulcers on a diagram of different diameter circles. The maximum score was 20 to accommodate the small number of RAS cases in which ulcers are on average more than 10mm in diameter.
3. **Duration:** The score corresponds to the average ulcer duration calculated in 1/2 week units; ie. ulcers lasting 10-11 days (1/2 weeks) will score 3 and an ulcer lasting five weeks or more will score the maximum of 10.
4. **Ulcer-free period:** The score for this parameter is 10 minus the average ulcer-free period in weeks; ie. somebody who is never free from ulcers will score the maximum 10, but somebody who is ulcer- free for four weeks at a time will score 6.
5. **Site:** The sites that are *usually* affected by the ulcers are recorded. A score of 1 is given to each of the non-keratinised sites (ie. labial mucosa, buccal mucosa, buccal sulcus, soft palate, ventral surface of the tongue, lateral border of the tongue, floor of the mouth). A score of 2 is given to each of the keratinised and specialised mucosal site affected (ie. hard palate, attached gingiva, alveolar ridge, dorsum of the tongue, tonsils, pillars of fauces, uvula, oropharynx). The site score is the combined score of all the keratinised and non-keratinised sites affected.
6. **Pain:** The pain associated with a crop of ulcers was estimated subjectively by the patient on a scale of 0 to10. A score of 1 was given if the ulcers caused a slight discomfort only and 10 if the pain was excruciating interfering with sleeping, eating and talking.

The total score is the summation of the six parameters scores. On the first visit, patients were asked to keep a diary of subsequent ulcer attacks to increase accuracy.

This method was appraised before it was introduced as apart of routine clinical practice. Twenty RAS subjects were assessed and scored blindly by two different clinicians. The mean score was 34 for clinician A and 33 for clinician B. The mean covariance in the total score was 8.5. The variation for each of the parameters was analysed and the results showed the inter-examiner covariance was 0.5 for the number of ulcers, 1.9 for the size of ulcers, 0.3 for the duration, 0.1 for the ulcer-free period, 2.2 for pain and 3.7 for the site. Subsequent changes to the form improved the latter to 3.1.

To demonstrate the effectiveness of the USS, 247 patients complaining of recurrent oral ulceration were examined on their first visit to the department of Oral Medicine and Pathology, Guy's Hospital, London. The

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ULCER SEVERITY SCORE (USS)
Recurrent Aphthous Stomatitis

Name:

Diagnosis:

Date of birth:

First visit to the department
Yes ☐ No ☐

Hospital number:

Patient on medication for RAS
Yes ☐ No ☐

Date:

Name of RAS medication:

Clinician:

Duration on medication:

	Ulcer characteristics	Score	Description of USS
Average **number** of ulcers			Score = average number of ulcers in a crop Maximum score = 20
Average **size** of ulcers (in mm)			Score = average size of ulcers in mm Maximum score = 20
Average **duration** of ulcers (in weeks)			Score = number of ½ weeks i.e. Half a week (3 days) scores 1, one and a half week (10 days) scores 3. Maximum score = 10
Ulcer-free period (in weeks)			Score = 10 minus the average ulcer-free period in weeks Maximum score = 10 (never free from ulcers)
Pain as perceived by the patient (on a scale of 0-10)			1 for slight discomfort when ulcers are present.10 for excruciating ulcers interfering with eating, and talking Maximum score = 10
Mucosal **site**	**Group 1** Labial mucosa Buccal mucosa Buccal Sulcus Soft palate Ventral of tongue Floor of mouth **Group 2** Hard palate Attached gingiva Alveolar ridge Dorsum of tongue Tonsils Pillars of fauces Uvula Oropharynx		Score = total of sites affected 1 for each site in group 1 (non-keratinised mucosa) 2 for each site in group 2 (keratinised, specialized) Maximum score = 10

Evidence of scarring Yes ☐ No ☐

Total USS:

Fig. 1 The ulcer severity scoring system form.

diagnosis of RAS into major, minor or herpetiform RAS was made according to the criteria described by Lehner (1968) (Table 1) before scoring the severity. Routine haematological tests carried out included full blood count, red blood cell folate, serum ferritin and serum vitamin B12. Twenty-four patients had atypical ulcers, systemic disease or abnormal blood results and therefore were excluded from the study. Two hundred and twenty three subjects were diagnosed with one type of RAS as follows:

1. Minor RAS: 136 subjects, aged 7-67 years, 81 females and 55 males.
2. Major RAS: 72 subjects aged 12-68 years, 42 females and 30 males.
3. Herpetiform RAS: 15 subjects aged 14-45 years, 13 females and two males.

All subjects were therefore diagnosed as having had one of the subtypes of RAS without apparent underlying systemic disease. The age range was wide and the duration of disease varied from a few months to many years. None were on medication for their oral ulcers when first recruited for the study. The diagnosis of one of the three types of RAS was made by oral medicine trained clinicians according to the history and clinical examination, and independent of the ulcer severity score. A standardised form (Fig 1) was used by the clinician to record the ulcer characteristics and the severity of the disease in the last three months prior to the visit.

Seventy-nine of the above subjects (41 minor and 38 major RAS) were scored again after three months treatment with topical steroids. These subjects were 12- 67 years of age, 47 females and 32 males. The regime they were on was the departmental standard therapy of betamethasone 500 microgram tablets dissolved in 10ml of water and used as a mouthwash for three minutes (Challacombe and Shirlaw, 1991) administered four times daily when ulcers are present and twice a day in between ulcer attacks.

RESULTS

Major, Minor and Herpetiform RAS

The scores for the minor RAS group (n=136) were between 18 and 43 with a mean (±SD) of 29.2 ±5.3. The mean score was significantly less than in the major RAS group (n=72, range: 28-60, mean 39.9 ±6.1, $p<0.001$) (table 2). The herpetiform RAS score range was wider between 18-57 with a mean of 36.6 ±8.4 (Table 2, Fig 2). There was an overlap in the score of major and minor RAS, concentrated between the scores of 28 and 43 (Fig 2).

Using binary logistic regression analysis, the total score was shown to be discriminative between minor and major RAS. There was a very good strength of agreement (92%) between the total score and the diagnosis (minor and major) (kappa=0.81). The individual ulcer characteristics were compared in the three types of RAS (Table 3). The score for all parameters examined except pain, were significantly greater in the major RAS group compared with the minor RAS group ($p<0.001$, Table 3).

An analysis of the distribution of the scores for each individual ulcer characteristic in the three groups of RAS showed that the herpetiform subjects had on average significantly more ulcers in an attack compared with major and minor RAS group ($p<0.001$). The major RAS group reported having on average significantly larger and more ulcers than the minor RAS group ($p<0.001$).

Table 1 Characteristics of the three main types of recurrent aphthous stomatitis

	Major	Minor	Herpetiform
Number	1-10	2-5	10-100
Size (mm)	>10	3-5	1-2 (but coalesce)
Peak age of onset (years)	5-20	10-20	20-30
Duration (weeks)	2-6	1-2	1-3
Scarring	+	-	+/-
Mucosal site	keratinised & non-keratinised	non-keratinised	any site, especially floor of the mouth

After Lehner (1968)

Table 2 Ulcer severity scores for the three types of recurrent aphthous stomatitis

	Major (n=136)	Minor (n=72)	Herpetiform (n=15)
Range	18-43	28-60	18-57
Mean (±SD)	29.2 (±5.3)	39.9 (±6.1)*	36.6 (±8.4)*
Median	29	40	37

* p<0.01 compared with the minor RAS group

Table 3 A comparison of the individual ulcer characteristics in the three types of recurrent aphthous stomatitis (mean ±SD)

Ulcer characteristics	Minor RAS (n=136) Mean ± SD	Major RAS (n=72) Mean ±SD	Herpetiform RAS (n=15) Mean ±SD
Number	3.7 ± 2.0	5.8 ± 3.5*	10.8 ± 6.7*
Size	5.6 ± 2.2	8.8 ± 3.3*	5 ± 2.9
Duration	3.5 ± 1.7	5.5 ± 2.5*	3.6 ± 1.8
Ulcer-free period	6.8 ± 2.9	7.8 ± 2.3*	7.5 ± 2.2
Pain	5.9 ± 1.7	6.2 ± 1.9	5.3 ± 1.2
Site	3.2 ± 1.8	5.3 ± 1.5*	5 ± 2.5*

* p<0.01 compared with the minor RAS group

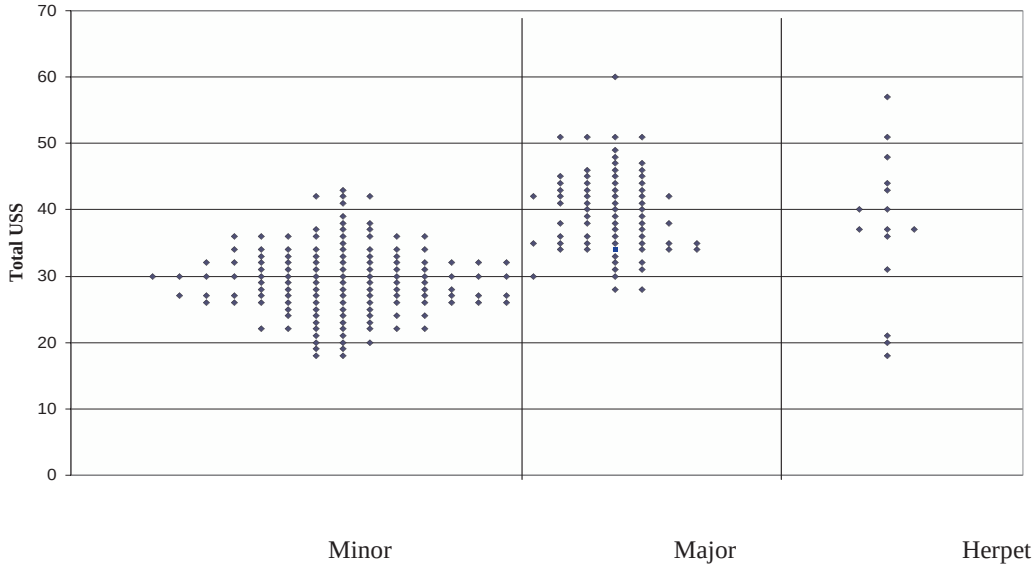


Fig. 2 A comparison of the Total Ulcer Severity Score in Minor, Major and Herpetiform Recurrent Aphthous Stomatitis.

RESPONSE TO TREATMENT

The mean ulcer severity score decreased significantly after three months topical steroid treatment from 34.6 ±7.1 to 27.4 ±11 ($p<0.001$). When the ulcer parameter scores were analysed separately, the results showed that for the 79 subjects studied, the score for the number, size, duration, site and pain were significantly less after three months treatment ($p<0.005$, Fig 3).However, the scores for the average ulcer-free period did not change significantly with treatment.

The mean percentage change in the USS was 20% (Fig 4). The USS improved in 30/79 (38%) subjects by at least 20%. In 19/79 (24%) subjects the USS remained the same or became slightly higher. Six patients (8%) had no recurrence of the ulceration within three months after commencing the treatment.

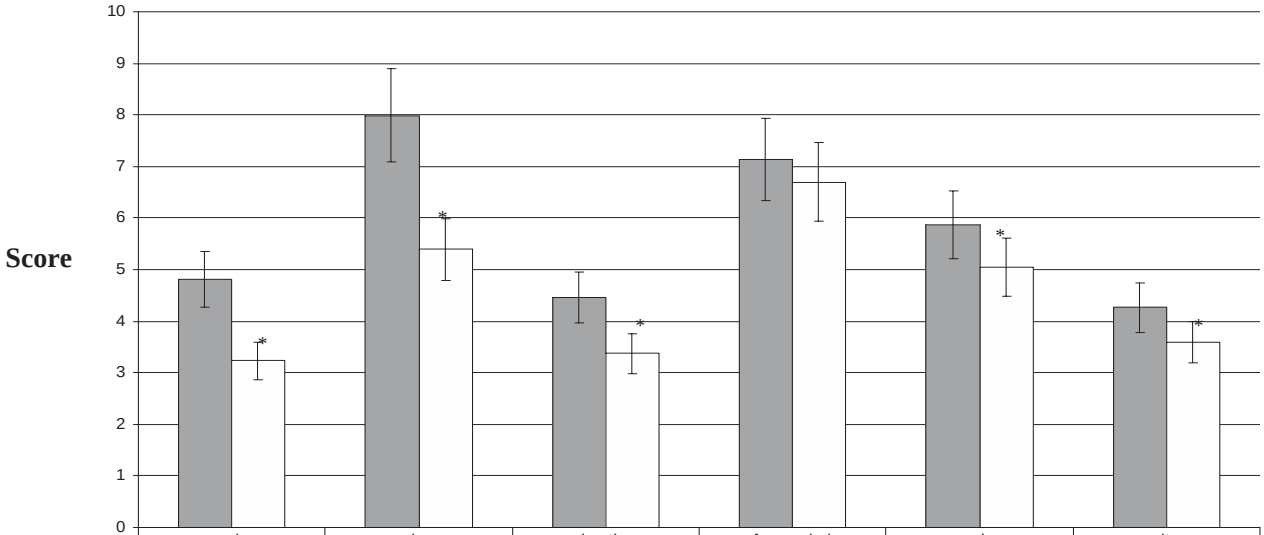
DISCUSSION

We describe in this paper a standardised assessment for an ulcer severity score (USS), which have been in routine use on our clinic for over two years. We have found that the form has helped in achieving consistency in history taking (which can be an issue with the rapid turn over of junior staff in hospitals) and that the application of the USS has helped in the systematic management of patients. Insignificant change of the USS is frequently an implication of a lack of response to treatment and an indication to revise the treatment plan and/or diagnosis.

The USS was found to be easy to use, readily applicable to a wide range of RAS subjects, reflects the disease severity and to be sensitive to clinical change with treatment.

By the nature of the condition studied, dependence on the patient's observations to describe the ulcer attacks is inevitable. However, using this method increased the reliability of the clinical information and improved the uniformity with which the questions were asked. Whenever possible, clinical examination and diaries were used to validate the history given by the patient.

The maximum score for each parameter was set to an upper limit that permitted the use of the full scale and was designed to incorporate at least 95% of clinical presentations in each category whilst not giving undue weight to a single parameter. This premise was supported by the analysis of 223 RAS patients (136 minor, 72 major and 15 herpetiform). The majority of the subjects had on average 10 or less ulcers in an attack, nine had 11-20 ulcers in a crop (five major RAS and four herpetiform) and three herpetiform subjects had more than 20 ulcers at a time. The maximum score for the number ulcers (set at twenty) embraced 220/223 clinical cases. Only six of the major RAS group had ulcers with an average size of greater than 10mm, including one with an average size of more than 20mm. It was perceived necessary that the scoring system should allow for ulcers that are larger than 10mm, not only to illustrate their severity but also to reflect change in the



	number	size	duration	free period	pain	site
Before Tx	4.81	7.99	4.46	7.14	5.86	4.27
After Tx	3.23	5.39	3.37	6.7	5.05	3.59

* $p<0.01$ compared with the minor RAS group

Fig. 3 Comparison of Individual Ulcer Characteristics before and after treatment.

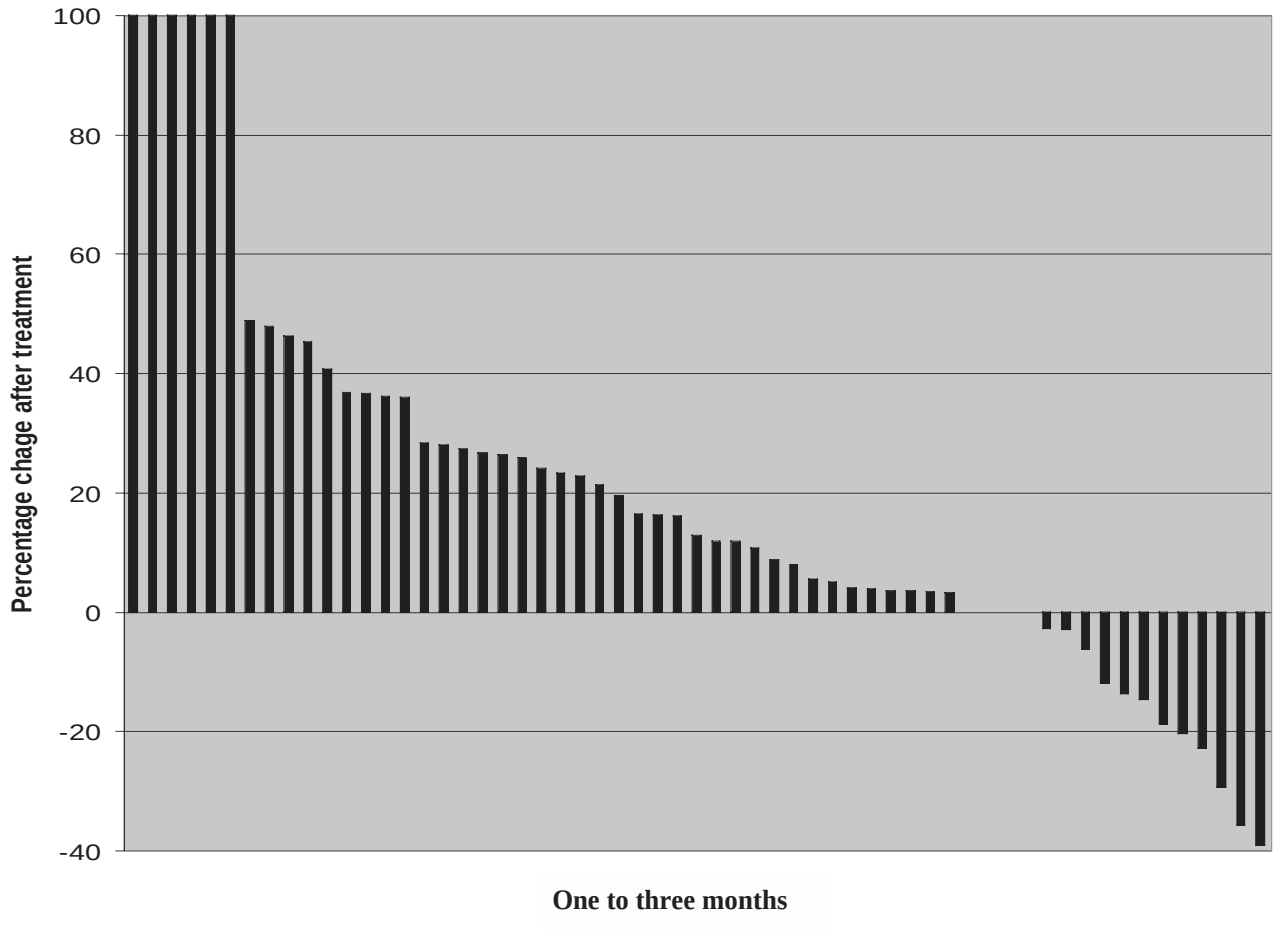


Fig. 4 Percentage change in the Ulcer Severity Score after three months treatment with betamethasone mouthwash.

condition with treatment. Thus an improvement of 50% in the diameter of 20mm ulcers would be expressed when comparing the score before and after treatment, whereas this would have not been the case if the maximum for this parameter had been only 10.

The duration of ulcers was scored in half- week units, as using days might have given undue weighting to this parameter and using weeks would not be sufficiently sensitive.

By using half-week units, an ulcer lasting 10 days will score 3. Out of the 223 RAS subjects studied, 11 (4.9%) had ulcers lasting more than five weeks so by having the maximum for this parameter at 10 (five weeks duration), 95% of the RAS presentations were included.

The shorter the ulcer-free period, the higher the score should be on the severity scale. The score for this parameter was therefore worked out as 10 (the maximum for this parameter) minus the ulcer-free period in weeks. Patients vary from having virtually continuous ulceration (score 10) to having three ulcer attacks a year with several months of ulcer-free period in between (score 0). Only four (1.7%) had an ulcer-free period of more than five weeks.

The overall results substantiate the generally accepted premise that greater than 95% RAS ulcer are: less than 20 in an attack, less than 20mm in diameter, last less than five weeks and recur at intervals of less than 10 weeks.

It was observed that the inclusion of "site" on the form helped in distinguishing between the subtypes of RAS. Most of the major RAS affect both keratinised and non-keratinised mucosa thus giving a higher score than the minor RAS, which usually affect only non-keratinised mucosa. Our results show that both the sites affected by ulcer attacks and the number of sites affected may change with treatment, consolidating the rationale for including this parameter.

Pain estimation is completely subjective as it is not yet possible to determine how much of reported pain is a result of stimulation or emotion in the single subject. Nevertheless, the estimation of pain is very important in the initial evaluation of disease severity as well as the

follow up process to determine efficacy of treatment (Conti et al, 2001; Linton and Gotestam, 1983). At present, there is no "standard" for quantifying pain and the available methods vary greatly (Downie et al, 1978). In a study aimed to evaluate the precision of four different pain rating scales (visual analogue, numerical, behaviour, and verbal scale) Conti et al (2001) reported that all four scales examined have the capacity to reflect change in pain intensity with treatment. However, only the numerical scale showed high correlation between two initial measurements of pain before commencement of treatment indicating precision and reproducibility of this scale. The pain measurement used in the present study was the numerical scale that initiates in 0 for no pain and ends in 10 when there is excruciating pain interfering with sleeping, eating and talking (Downie et al, 1978).

The diagnosis of RAS should be clinically based. The proposed USS is designed for the assessment of disease severity not for diagnosis. Nevertheless, the results show that the proposed USS was able to largely discriminate between major and minor RAS (kappa=0.81) (Fig 2). The mean USS for the minor RAS group was significantly less than that of the major RAS subjects (Table 2). However, there was an overlap in the range for minor RAS and major RAS scores concentrated between the scores of 28 and 43 (Fig 2). This can at least partially be explained by our study subject group, who were specialist clinic attendees and probably had the more severe variety of minor RAS. Despite this overlap there was a very good strength of agreement (92%) between the total score and the diagnosis. There were significant differences between the minor RAS and the major RAS groups in the scores of all the individual parameters except pain (Table 3).

The comparison of the USS before and after treatment showed significant reduction in the mean score, implying that this method is sensitive enough to reflect changes in the severity of disease and maybe useful in determining the efficacy of therapy. The possibility of analysing the scores for each of the USS parameters independently may be of value in determining the effect of therapy on the individual ulcer characteristics. In the present investigations the results suggested that three-month regime with betamethasone mouthwash will significantly reduce the number, size, duration, sites and pain ($p<0.005$, Fig 4). Evidently, for more accurate interpretation of the effect of therapy on RAS, randomised placebo controlled trials are necessary.

There is no substitute for good clinical judgement in the diagnosis and management of oral disease. However, in the era of evidence-based dentistry, the presence of a uniform method of evaluating disease severity might prove valuable in aiding the management of RAS and encouraging research and clinical trials.

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