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Randomized, double-blind, placebo-controlled trial of oral aloe vera gel for active ulcerative colitis

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SUMMARY

Background: The herbal preparation, aloe vera, has been claimed to have anti-inflammatory effects and, despite a lack of evidence of its therapeutic efficacy, is widely used by patients with inflammatory bowel disease.

Aim: To perform a double-blind, randomized, placebo-controlled trial of the efficacy and safety of aloe vera gel for the treatment of mildly to moderately active ulcerative colitis.

Methods: Forty-four evaluable hospital out-patients were randomly given oral aloe vera gel or placebo, 100 mL twice daily for 4 weeks, in a 2 : 1 ratio. The primary outcome measures were clinical remission (Simple Clinical Colitis Activity Index $\leq$ 2), sigmoidoscopic remission (Baron score $\leq$ 1) and histological remission (Saverymuttu score $\leq$ 1). Secondary outcome measures included changes in the Simple Clinical Colitis Activity Index (improvement was defined as a decrease of $\geq$ 3 points; response was defined as remission or improvement), Baron score, histology score, haemoglobin, platelet count, erythrocyte sedimentation rate, C-reactive protein and albumin.

Results: Clinical remission, improvement and response occurred in nine (30%), 11 (37%) and 14 (47%), respectively, of 30 patients given aloe vera, compared with one (7%) [$P = 0.09$; odds ratio, 5.6 (0.6–49)], one (7%) [$P = 0.06$; odds ratio, 7.5 (0.9–66)] and two (14%) [$P < 0.05$; odds ratio, 5.3 (1.0–27)], respectively, of 14 patients taking placebo. The Simple Clinical Colitis Activity Index and histological scores decreased significantly during treatment with aloe vera ($P = 0.01$ and $P = 0.03$, respectively), but not with placebo. Sigmoidoscopic scores and laboratory variables showed no significant differences between aloe vera and placebo. Adverse events were minor and similar in both groups of patients.

Conclusion: Oral aloe vera taken for 4 weeks produced a clinical response more often than placebo; it also reduced the histological disease activity and appeared to be safe. Further evaluation of the therapeutic potential of aloe vera gel in inflammatory bowel disease is needed.

INTRODUCTION

Aloe vera is a stemless, drought-resisting succulent of the lily family. It is indigenous to hot countries and has been used medicinally for over 5000 years by Egyptian, Indian, Chinese and European cultures. Aloe vera gel is the mucilaginous aqueous extract of the leaf pulp of *Aloe barbadensis* Miller. It contains over 70 biologically active compounds and is claimed to have anti-inflammatory, anti-oxidant, immune boosting, anti-cancer, healing, anti-ageing and anti-diabetic properties.[1] Aloes, by contrast, is an anthraquinone derivative of the sap of

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the aloe leaf which has been used for centuries as a purgative.

Aloe vera gel is widely promoted for the treatment of digestive disorders, skin diseases and wound healing. Although there is, as yet, little scientific evidence to support these claims, *in vitro* studies have shown that aloe vera has anti-oxidant and other anti-inflammatory effects (see 'Discussion' section), and a randomized trial has shown that topical aloe vera gel is superior to placebo in the treatment of plaque psoriasis.[2]

Because conventional therapies for inflammatory bowel disease are not always successful in achieving remission or preventing relapse, and may cause serious side-effects, up to 50% of patients seek alternative options.[3–5] In our own survey, aloe vera was the single most widely used herbal therapy.[6] This, and the beneficial effect of aloe vera in psoriasis, led us to investigate the efficacy and safety of oral aloe vera gel, given for 4 weeks, in a randomized, double-blind, placebo-controlled trial in patients with mildly to moderately active ulcerative colitis.

METHODS

Patient selection

Patients who met the inclusion criteria shown below and consented to participate were consecutively recruited at Barts and The London NHS Trust, London, and the John Radcliffe Hospital, Oxford, between March 1999 and July 2003. The diagnosis of ulcerative colitis was confirmed by standard clinical, radiological, endoscopic and histological criteria prior to inclusion in the trial; demographic and clinical details are shown in Table 1. The Ethics Committee at each centre approved the study. Patients gave written informed consent and the study was conducted according to the principles of the Second Declaration of Helsinki.

The trial profile is shown in Figure 1. The inclusion criteria were an age of 18–80 years, mildly to moderately active ulcerative colitis [as defined by a modified (see below) Simple Clinical Colitis Activity Index (SCCAI) ≥ 3][7] and no recent changes in conventional prophylactic therapy (see below).

The exclusion criteria were as follows: acute severe ulcerative colitis requiring hospital admission (SCCAI > 12); inactive disease (SCCAI < 3); positive stool examination for pathogens; Crohn's disease or indeterminate colitis; use of antibiotics, warfarin, cholestyramine, sucralfate, anti-diarrhoeal drugs (loperamide, codeine phosphate, diphenoxylate), non-steroidal anti-inflammatory drugs, aspirin > 75 mg/day, aloe vera or other herbal remedies; alcohol or drug abuse; pregnancy or breast feeding; female of child-bearing age not taking adequate contraception; participation in another drug trial in the previous 3 months; and serious liver, renal, cardiac, respiratory, endocrine, neurological or psychiatric illness. Patients were also excluded if they had altered their dosage of aminosalicylates in the previous 4 weeks, had taken > 10 mg/day or had altered their oral prednisolone dosage in the previous 4 weeks, had

Table 1. Demographic details of patients recruited to the trial

	Aloe vera ($n = 30$)	Placebo ($n = 14$)
Age (years) (median, range)	40 (22–76)	36 (20–55)
Sex (male : female)	16 : 14	6 : 8
Disease extent		
Proctitis	4	3
Distal	8	5
Left-sided	12	3
Sub-total	2	2
Total	4	1
Concurrent therapy		
5-ASA	20	8
Prednisolone	0	0
Azathioprine	1	2
Topical 5-ASA	1	0
Topical steroid	3	3
None	10	5

5-ASA, 5-aminosalicylic acid.

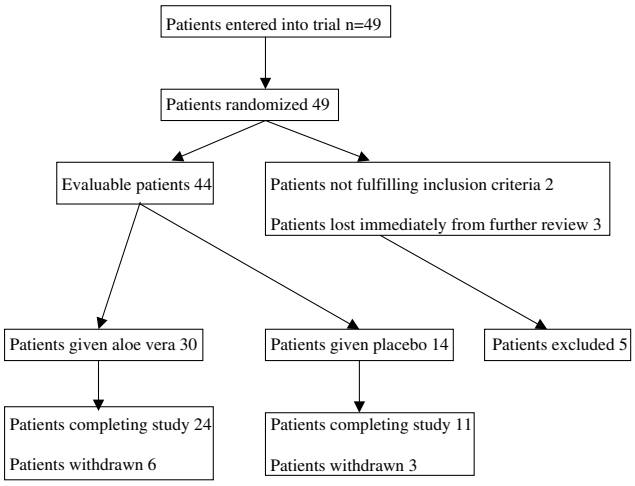

Figure 1. Trial profile.

changed their dose of azathioprine or 6-mercaptopurine in the previous 3 months, or had used more than five corticosteroid or aminosalicylate enemas in the previous 2 weeks.

Trial medication

Treatments consisted of a liquid to be taken orally. The active treatment was aloe vera gel (kindly provided by Dr Peter Atherton, Forever Living Products, Jersey, Channel Islands). The placebo consisted of a liquid preparation containing flavourings, but no known active agents (synthesized by Flavex International Ltd, Hereford, UK), which was identical in taste and appearance to the aloe vera preparation. The dose used was 100 mL twice daily, this being the maximum dose tolerated and commonly employed by individuals using aloe vera gel for a range of indications. Patients were advised to start with 25–50 mL twice daily for up to 3 days to ensure tolerability and to minimize the risk of side-effects. The daily dosage of trial medication was recorded by participants on their daily symptom diary card (see below).

Trial protocol

Eligible patients were interviewed and informed of the details of the trial verbally and in writing. Those agreeing to participate were issued with a written information sheet prior to signing a consent form. They underwent history review and physical examination and were issued with a symptom diary card for the SCCAI (see below); a stool specimen was sent for culture for pathogens, including *Clostridium difficile* (Figure 1).

Patients were reviewed after 1 week (i.e. at week 0 of the treatment period). Those meeting the inclusion criteria were randomized by a trial pharmacist at Barts and The London NHS Trust, using a computer-generated, block-design, randomization sequence, to receive active herbal remedy or placebo; a ratio of 2 : 1 for aloe vera : placebo was employed.

Patients completed the Inflammatory Bowel Disease Questionnaire (IBDQ) for the quality of life.[8] At the same visit, rigid sigmoidoscopy was performed and mucosal appearances were assessed using the Baron score.[9] A rectal biopsy was taken for histological scoring of disease activity.[10] The SCCAI for the preceding week, blood count, routine biochemistry including serum albumin concentration, C-reactive protein and erythrocyte sedimentation rate were measured. Diary cards were issued for the next 2 weeks. Aloe vera or placebo was dispensed with instructions about dosage. Patients were instructed to continue any long-term prophylactic medication (see inclusion criteria above) unaltered throughout the 4-week trial.

Patients were reviewed at 2 and 4 weeks after starting treatment. At each visit, diary cards were collected to calculate the SCCAI and to record compliance with the study medication. The interviewing doctor made a global assessment of disease activity (physician's global assessment, scored thus: much better, + 2; slightly better, + 1; the same, 0; slightly worse, − 1; much worse, − 2). Blood count and routine biochemistry were checked for safety purposes. After 4 weeks of treatment, all the procedures undertaken at weeks 0 and 2 were repeated.

Criteria for withdrawal

To minimize the risk of adverse effects of the trial medication on their well-being, patients were withdrawn if, at any time, they or their physician believed that they had deteriorated substantially. These patients were then given topical or oral conventional therapy. Patients who were withdrawn were offered continued follow-up in the out-patient clinic to ensure their well-being and the absence of side-effects of the study medications.

Measurement of clinical disease activity

Disease activity scores were calculated using the SCCAI.[7] This was modified to allow inclusion of patients with active proctitis, but without increased stool frequency. The modification involved altering the scores for stool frequency so that patients recording zero or one bowel movement in a day scored zero, those with 2–3 stools scored 1 point, those with 4–6 scored 2, those with 7–9 scored 3 and those with > 9 scored 4. To confirm the validity of this minor modification, we showed that, in patients at baseline, the SCCAI was significantly negatively correlated with the IBDQ[8] ($R = -0.63$, $P < 0.0001$); it also correlated positively with the Baron sigmoidoscopic score[9] ($R = +0.35$, $P < 0.03$).

Outcome measures

The primary outcome measures were clinical remission (defined as SCCAI ≤ 2), sigmoidoscopic remission

[Baron score of zero (normal-looking mucosa) or one (mucosal oedema as indicated by loss of the normal vascular pattern)][9] and histological remission (Saverymuttu score of ≤ 1, i.e. no loss of colonocytes, absence of crypt inflammation, and normal lamina propria content of mononuclear cells and neutrophils).[10] All histological grades were assessed by the same experienced histopathologist (RMF) blind to the treatment given.

The secondary outcome measures included changes in the clinical condition, assessed by the SCCAI (improvement defined as a reduction in score of ≥ 3 points; response defined as remission or improvement), physician's global assessment and IBDQ; changes in the sigmoidoscopic score (improvement defined as a decrease of ≥ 2 points) and histological score (improvement defined as a decrease of ≥ 3 points); and changes in laboratory measures of inflammation, haemoglobin, platelet count, erythrocyte sedimentation rate, C-reactive protein and albumin.

Possible adverse effects of the trial medications were also recorded.

Power calculations and statistical analysis

On the assumption of a 10% clinical remission rate with placebo[11] and a 50% remission rate with aloe vera gel, and with the use of a 2 : 1 aloe vera : placebo randomization scheme, 45 patients were required to detect this difference at the 5% level of significance (two-tailed) with 80% power. All patients who met the inclusion criteria and were effectively followed up were included in the analyses.

Fisher's exact test was used to compare treatment and placebo groups with respect to gender. The chi-squared test was used to compare treatment and placebo groups in relation to baseline disease extent and therapy. The Mann–Whitney *U*-test was used to compare the groups at baseline in relation to age, SCCAI, IBDQ, sigmoidoscopic score, histological grade and blood results. Correlations at baseline between SCCAI, IBDQ and sigmoidoscopic score were assessed by Spearman's rank correlation test.

Fisher's exact test was used to compare the proportions of patients in each group who achieved clinical, sigmoidoscopic or histological remission, improvement or response after 4 weeks. Odds ratios (with 95% confidence limits) were calculated to compare the effects of aloe vera and placebo. For each treatment group, the Wilcoxon signed rank test was used to assess changes from baseline to week 4 in SCCAI, IBDQ, physician's global assessment, sigmoidoscopic score, histological grade and blood test results. Where data at the week 4 visit were missing because of earlier patient withdrawals or other reasons, the last-value-carried-forward technique was used. All analysis was undertaken on an intention-to-treat basis.

Statistical calculations were made using computer software programs (Microsoft Excel and GraphPad Prism 3.02). Numerical results are expressed as the median and interquartile range. Because all the comparisons to be made were planned prospectively, no correction for multiple comparison was applied.[12] All tests were two-tailed and significance was reported at the 5% level.

RESULTS

Patients at baseline

The flow of the patients through the trial is shown in Figure 1. Of the 49 patients assessed and entered into the trial, five were excluded from further analysis after randomization. Of these, two patients were found, on analysis of their case record forms, to have inactive disease at entry (SCCAI = 1) and three patients failed to return for review after the trial consultation at week 0 despite repeated attempts to make contact with them. Forty-four evaluable patients were therefore randomly given aloe vera gel ($n = 30$) or placebo ($n = 14$). There were no significant differences between the two treatment groups at baseline in relation to age, gender, disease extent, current conventional therapy, disease activity, sigmoidoscopic score, histological grade or laboratory results (Tables 1–3).

Patient withdrawals

Six patients (20%) given aloe vera gel and three patients (21%) given placebo withdrew from the study because of deterioration or a failure to improve sufficiently. Variables recorded at the time of their withdrawal were included in the data analyses shown below.

Clinical outcome

After 2 weeks of therapy, clinical remission (SCCAI ≤ 2 points), improvement (fall in SCCAI of ≥ 3 points)

Table 2. Numbers of patients (%) given oral aloe vera gel and placebo showing clinical, sigmoidoscopic and histological remission, improvement and/or response

	Aloe vera	Placebo	*P*	OR (95% CL)
Clinical score (SCCAI)	$n = 30$	$n = 14$		
Remission (score ≤ 2)	9 (30%)	1 (7%)	0.09	5.6 (0.6–49)
Improvement (fall ≥ 3)	11 (37%)	1 (7%)	0.06	7.5 (0.9–66)
Response	14 (47%)	2 (14%)	0.048	5.3 (1.0–27)
Sigmoidoscopic score	$n = 26$	$n = 11$		
Remission (score 0–1)	7 (27%)	2 (18%)	0.69	1.7 (0.3–10)
Improvement (fall ≥ 2)	5 (18%)	1 (9%)	0.65	2.6 (0.3–25)
Histological score	$n = 21$	$n = 9$		
Remission (0–1)	6 (29%)	4 (44%)	0.43	0.5 (0.1–2.5)
Improvement (fall ≥ 3)	8 (38%)	3 (33%)	1.00	1.2 (0.2–6.4)

CL, confidence limit; OR, odds ratio; SCCAI, Simple Clinical Colitis Activity Index.
Numbers of patients for each measure vary as not all patients underwent follow-up sigmoidoscopy or rectal biopsy; numbers recorded (*n*) are those with paired data. *P* values (Fisher's exact test) and OR (95% CL) are shown.

Table 3. Numerical values of all measures assessed before and after 4 weeks of treatment with oral aloe vera gel or placebo

	Aloe vera		Placebo	
	Week 0	Week 4	Week 0	Week 4
SCCAI	6.5 (5.2–8.2)	6.0 (2.0–9.0)*	6.1(4.7–7.6)	4.9 (3.3–7.5)
IBDQ	4.4 (3.2–5.0)	4.8 (3.8–5.7)	4.6 (3.6–5.1)	5.8 (4.8–5.9)*
PGA	–	0 (− 1 to + 2)	–	+ 1 (0 to + 2)
Sigmoidoscopic score	3 (2–3)	2 (1–3)	3 (2–3)	2 (1.5–3)
Histological score	6.5 (3–8)	5 (1–8)*	6 (1.5–7)	5 (1–8)
Haemoglobin (g/dL)	13.0 (12.3–14.3)	13.0 (12.0–13.8)	13.3 (12.7–14.5)	13.3 (12.7–14.8)
Platelet count ($\times 10^9$)	301 (255–331)	299 (254–361)	300 (265–345)	300 (248–367)
ESR (mm/h)	12 (5–21)	9 (2–20)	9 (3–13)	10 (3–20)
CRP (mg/L)	5 (4–11)	4 (4–9)	5 (4–8)	4 (3–9)
Albumin (g/L)	44 (42–46)	43 (42–45)	44 (42–46)	43 (41–46)

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IBDQ, Inflammatory Bowel Disease Questionnaire; PGA, physician's global assessment; SCCAI, Simple Clinical Colitis Activity Index.
Medians (interquartile range) are shown.
* $P < 0.05$ from pre-treatment value.

and response were noted in three (10%), five (17%) and five (17%) patients taking aloe vera gel, but in no patients given placebo. These apparent differences did not reach statistical significance (data not shown).

Clinical remission (SCCAI ≤ 2 points) at 4 weeks occurred in nine of 30 patients (30%) given aloe vera gel, compared with one of 14 patients (7%) given placebo [$P = 0.09$; odds ratio (OR), 5.6 (0.6–49)] (Table 2, Figure 2). Clinical improvement after 4 weeks (fall in SCCAI of ≥ 3 points) was recorded in 11 patients (37%) on aloe vera and in one patient (7%) on placebo [$P = 0.06$; OR, 7.5 (0.9–66)]. Fourteen patients (47%) given aloe vera showed a clinical response at 4 weeks, compared with two (14%) of those taking placebo [$P = 0.048$; OR, 5.3 (1.0–27)]. The median SCCAI showed a small but statistically significant fall after 4 weeks of treatment with aloe vera ($P = 0.01$), but not with placebo (Figure 2).

The physician's global assessment showed no change during the treatment period in either patient group (Table 3). The IBDQ was also unaltered during 4 weeks of treatment with aloe vera. In contrast, in the eight placebo-treated patients who completed the IBDQ before and after the trial period, the median score rose significantly ($P = 0.03$); unfortunately, however, the three patients in the placebo group who withdrew from the trial failed to return the questionnaires they were issued at the time of withdrawal.

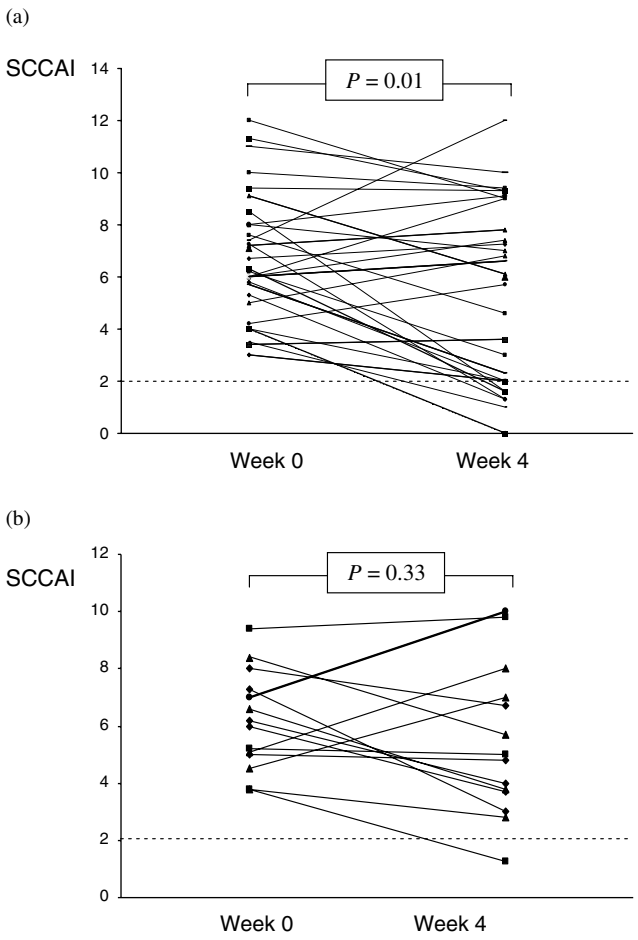

Figure 2. Changes in the Simple Clinical Colitis Activity Index (SCCAI) induced by 4 weeks of treatment with oral (a) aloe vera gel ($n = 30$) or (b) placebo ($n = 14$). The dotted line denotes the remission value for SCCAI ($\leq$ 2).

Sigmoidoscopic and histological appearances

There were no significant differences in the proportions of patients in the two treatment groups entering sigmoidoscopic remission (Baron score of 0 or 1) or showing sigmoidoscopic improvement (defined by a fall in Baron score of ≥ 2 points) (Table 2). The same was true for the histological scores (Table 2). However, although the sigmoidoscopic score showed no significant changes in either treatment group, the histological score fell significantly in patients given aloe vera gel for 4 weeks ($P = 0.031$) (Table 3).

Laboratory measures of disease activity

Neither aloe vera gel nor placebo had a significant effect on the patients' haemoglobin, platelet count, C-reactive protein or serum albumin concentration, most of which were normal or only marginally abnormal on recruitment to the study (Table 3).

Adverse effects

Adverse effects recorded in the patients taking aloe vera gel and placebo were minor, similar and not clearly related to the study medications. Of the 30 patients randomized to aloe vera gel, one complained of abdominal bloating, one of pain in her feet, one of sore throat, one of transient ankle swelling, one of acne and one of worsening eczema. Of the 14 patients taking placebo, two reported bloating, one foot pain and one acne. No patients developed abnormal blood tests attributable to aloe vera gel or placebo, or were withdrawn from the trial because of adverse effects.

DISCUSSION

Herbal therapies in general, and aloe vera in particular, are already widely used by patients with inflammatory bowel disease.[3–5] Previous clinical trials of varying design and accessibility have claimed that *Boswellia serrata*[13] and several traditional Chinese medical approaches are beneficial in active ulcerative colitis.[14, 15] In this randomized, double-blind, placebo-controlled clinical trial, treatment for 4 weeks with oral aloe vera gel produced a symptomatic clinical response more frequently than did placebo. In addition, the clinical (SCCAI) and histological disease activity scores fell in the aloe vera-treated group of patients, but not in those given placebo. The magnitude of the effect of aloe vera, as indicated by a clinical response rate of nearly 50%, and an odds ratio over placebo of over five, resembles that reported for mesalazine in a meta-analysis.[16]

The sample size and power calculation for this study were influenced by our desire to restrict to a minimum the number of patients needed to be treated with aloe vera or placebo in order to obtain a meaningful result. At the outset, we had no pointers as to either the therapeutic efficacy or safety of aloe vera in patients with active ulcerative colitis. To minimize the number of patients exposed to aloe vera, were it to prove to be ineffective or unsafe, we decided to use a placebo-controlled trial design rather than one using an active comparator, such as mesalazine. In order to minimize the number of patients given placebo, we used a 2 : 1

aloe vera to placebo ratio, aiming for an absolute improvement in outcome of 40% for the active over placebo treatment.

In some trials in inflammatory bowel disease, the response (as opposed to remission) rate in patients given placebo has approached 50%. However, in designing this trial in 1998, we focused specifically on the placebo-related remission rate in out-patients with active ulcerative colitis. In the event, our placebo rate for remission (7%) closely resembled the 10% figure which was taken for our power calculations from the meta-analysis published in 1997 of 44 placebo-controlled trials in out-patients with active ulcerative colitis.[11]

In retrospect, it is to be regretted that our trial was not larger, as the clinical remission and improvement rates on aloe vera gel failed to reach statistical significance. Nevertheless, several factors support the view that aloe vera has a genuine, albeit modest, anti-inflammatory therapeutic effect in mildly to moderately active ulcerative colitis. First, there was a trend in favour of aloe vera for these two variables at 2 weeks as well as at 4 weeks. Second, the improvement in SCCAI after 4 weeks of aloe vera covered all the domains of the scoring system, and was not due solely, for example, to a reduction in stool frequency, as might have occurred with a constipating agent such as loperamide. Third, the histological scores showed a small, but statistically significant, improvement in patients given aloe vera for 4 weeks. Finally, the sigmoidoscopic appearances also showed a trend in favour of aloe vera at 4 weeks. In the latter context, the standard scoring system which was used to assess the mucosal appearance macroscopically is known to be prone to inter-observer variability at its lower grades:[10] this factor could conceivably have prevented the detection of a significant improvement in this small study.

Despite the significant inverse correlation between SCCAI and IBDQ scores pre-treatment, the improvement (rise) in median IBDQ in the aloe vera gel-treated patients failed to reach statistical significance. This finding may represent a type 2 statistical error, as the trial was not powered specifically for changes in IBDQ. Conversely, as indicated in the 'Results' section, the apparent improvement in quality of life in the placebo-treated subjects is likely to have been a consequence of incomplete IBDQ data collection in the individuals withdrawing from the trial prematurely.

Because the trial was small, sub-group analysis was inappropriate. However, there was no obvious relation between response to aloe vera and disease activity at recruitment, disease extent and use, or not, of concurrent conventional medications.

The preparation of aloe vera given in this trial is reported to contain a high proportion (> 95%) of the active ingredient, namely the pulp of the leaf of the aloe vera plant; some commercially available preparations contain far less (International Aloe Science Council, http://www.iasc.org).[17] The dose of aloe vera gel used in this trial was the maximum recommended by the manufacturers, and was at the top of the range of doses used and tolerated by the large numbers of individuals taking this agent for this and other indications. It is conceivable, however, that a higher dose might have been more efficacious, albeit possibly at the expense of more side-effects, of which none of note occurred during this trial. Conversely, any conclusions drawn from this study cannot necessarily be extrapolated to other preparations or lower doses of aloe vera.

The mechanisms by which aloe vera gel may act are unclear. *In vivo*, aloe vera reduces irritant-induced production of inflammatory mediators in paw, ear and synovial models of inflammation in animals.[18–20] Aloe vera gel and its components also ameliorate ultraviolet-induced immune suppression.[21–24]

In vitro, several fractions of aloe vera, as well as the unfractionated whole gel, have anti-oxidant effects.[25–27] Aloe vera gel contains peroxidase activity,[28] several superoxide dismutase enzymes[29] and a phenolic anti-oxidant.[26]

Aloe vera appears to have various immuno-inhibitory effects. Extracts of the gel reportedly deplete complement in pooled human serum by an effect on the alternative pathway,[30] inhibit ultraviolet irradiation-induced release of tumour necrosis factor-α by human epidermoid carcinoma cells,[24] and reduce histamine and leukotriene release from guinea pig mast cells.[31]

Finally, and in contrast, aloe vera gel and one of its principal components, acemannan, have been reported to possess immuno-stimulatory properties. Acemannan up-regulates nitric oxide production by chicken spleen cells and HD11 cell lines, an effect mediated through mannose receptors.[32] In addition, acemannan stimulates the release of reactive oxygen metabolites, interleukin-1, interleukin-6 and tumour necrosis factor-α from murine macrophages.[33–35] Acemannan also promotes differentiation and maturation of dendritic cells[34] and increases human T-cell responsiveness to allo-antigen.[36]

In designing this trial, we were in agreement with pharmaceutical commentators[17, 37] and the Medicines Control Agency that there was an urgent need to evaluate formally the efficacy and safety of aloe vera gel in the treatment of ulcerative colitis. We felt that the demonstration of the efficacy of aloe vera, a 'natural' product, would be helpful for the many patients currently using herbal therapy and specifically this preparation. In contrast, a failure to show benefit, or the identification of adverse effects, would have resulted in advice to patients to avoid using this expensive product (up to £20 per week, depending on the dose and preparation used).

Our results are encouraging, although not conclusive. They indicate the need for further larger controlled trials of aloe vera gel, not only in moderately active ulcerative colitis, but also in the maintenance of remission in ulcerative colitis and in Crohn's disease; direct comparisons with mesalazine would be worthwhile. Until such studies are performed, patients with inflammatory bowel disease should be advised to exercise caution and, in particular, should not use aloe vera gel as an alternative to conventional therapy. Finally, it should be emphasized to potential users that any possible clinical benefits suggested by this trial are modest. Patients should also be made aware that this small study does not exclude the possibility of adverse effects of aloe vera, whether direct or as a result of hitherto unrecognized interactions with conventional medications.

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