Pilot study of the effect of individualised homeopathy on the pruritus associated with atopic dermatitis in dogs

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Twenty dogs with confirmed atopic dermatitis were treated with homeopathy. In the first phase of this pilot study, all of the dogs were treated by a veterinary homeopath with individualised remedies prescribed on the basis of the dog's cutaneous signs and constitutional characteristics. The response to treatment was assessed by scoring the severity of pruritus from 0 to 10 on a validated scale. The dogs were evaluated at monthly intervals for at least two months. In 15 cases, the owners reported no improvement following homeopathic treatment. In the other five cases, the owners believed that the homeopathic treatment was associated with a substantial improvement, and reported reductions in pruritus scores ranging from 64 to 100 per cent. These five dogs were selected for the second phase of the study, in which homeopathic remedies were tested against placebos in a randomised and blinded trial. In one of these dogs, atopic dermatitis resolved completely and so this dog could not participate in phase 2; another dog was euthanased because of status epilepticus before phase 2 could be started. In the remaining three cases, the owners correctly distinguished between the placebo and homeopathic remedies, and reported reductions in the pruritus score of 0, 0·2 and 0·8 following placebo treatment and 4·3, 2·4 and 3·0, respectively, following the remedy.

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THE practice of homeopathy is currently under great scrutiny in both the medical and veterinary fields, and no other form of treatment appears able to polarise opinions to such an extent (Baker and others 2005, Hektoen 2005a). Conventional medical practice dictates that the principle on which homeopathy is based has no grounding in science, and any response to treatment is discounted as pure placebo effect. However, trained medical and veterinary homeopaths maintain that their system, although not fully understood from a scientific point of view, yields genuine therapeutic results, often after conventional medical treatment has failed.

Two major problems prevent homeopathy from gaining widespread acceptance. The first, and most compelling, reason for disbelief is the nature of the remedies. To produce standard homeopathic medications, the source material is diluted repeatedly, often to such an extent that no molecules of it are likely to remain in the final solvent. The second reason is that evidence from clinical trials to demonstrate the efficacy of homeopathic remedies is extremely limited, particularly in veterinary medicine, and often hampered by poor trial design. Most homeopathic prescribing is based on 200 years of accumulated clinical experience, and reported outcomes can be greatly influenced by placebo and other non-specific effects, random variation, observer bias, regression to the mean (where exacerbations or severe forms of a disease naturally revert back to a more typical level) and spontaneous recovery. Such obstacles may appear insurmountable, leading some authors to conclude that the practice of veterinary homeopathy should cease (Baker and others 2005, Rijnberk and Ramey 2007).

However, both of the above problems are beginning to be addressed by the scientific community. Traditional chemical approaches state that the ultradilution of molecules in water beyond Avogadro's number will yield a final solution that is identical to the solvent. Although this seems logical to most scientists, materials scientists regard it as a simplistic way to view the complex interactions between solutes and the three-dimensional structure of water. Different homeopathic remedies and different dilutions of the same remedy have been distinguished from each other using Raman and infrared spectroscopy, even though all should contain nothing but water (Rao and others 2007). Such findings may relate to complex processes such as epitaxy (the transfer of information from the surface of a solid substance to a liquid) and the formation of colloidal nanobubbles during succussion, the process in which homeopathic remedies are 'pounded' with each successive dilution. Nanobubbles contain

gaseous inclusions of oxygen, nitrogen, carbon dioxide and possibly the remedy source material (Rao and others 2007). Hence, although there is still no plausible mechanism for a 'pharmacological' action of homeopathic remedies, a fixation on the fundamental problem of Avogadro's number may be inappropriate.

There is a lack of clinical evidence for the efficacy of homeopathic remedies compared with conventional medicines. To date, comprehensive meta-analyses of placebo-controlled trials in human medicine have, in general, suggested that homeopathy is superior to placebo, but have not demonstrated specific conditions for which homeopathy is clearly efficacious (Linde and others 1997, Ernst 2002). Reviews focusing on specific medical conditions have reported both positive (Taylor and others 2000) and negative (Ernst 1999) conclusions. In veterinary medicine, there have been few studies to evaluate treatment-specific effects of homeopathy, and most have addressed herd problems in farm livestock (Hektoen 2005b, Mathie and others 2007). To date, controlled trials of homeopathy published in the veterinary literature have not shown significant effects (Scott and others 2002, de Verdier and others 2003, Hektoen and others 2004, Holmes and others 2005, Cracknell and Mills 2008), but beneficial responses have been reported elsewhere (Searcy and others 1995, Albrecht and Schütte 1999). One obstacle to the performance of clinical trials to investigate veterinary homeopathy is the holistic approach taken by homeopathic practitioners, in which the whole patient is treated on the basis of the individual signs and constitutional characteristics, rather than just a specific disease. This makes the monitoring of appropriate outcome parameters difficult. However, if veterinary or medical homeopathy is to gain acceptance by conventional clinicians, it is essential that specific conditions are identified that may be helped by this mode of therapy.

This study reports the use of homeopathic methods in the treatment of atopic dermatitis in dogs, a well characterised condition with a specific clinical phenotype (Olivry and others 2001). This disease highlights some of the problems that can arise when clinical investigations are performed to evaluate the use of homeopathy. For example, a previous single-blinded, placebo-controlled study was conducted by an eminent team of veterinary dermatologists to determine the efficacy of a commercial homeopathic remedy in the treatment of canine atopic dermatitis (Scott and others 2002). Although no beneficial effects were seen, the study design was widely criticised by homeopathic practitioners who wrote to the journal in which the study was reported, claiming that the requirement for individualisation of remedies had been completely misunderstood and ignored by the authors (Drosdovech and others 2002, Jouppi 2002, Kujala 2002, Taylor 2002, Van As 2002). In contrast, a study undertaken by veterinary homeopathic practitioners reporting a moderate or major improvement in 56 per cent of dogs with atopic dermatitis (Mathie and others 2007) was non-controlled in nature, and can be criticised further because it did not use standardised methods of diagnosis, monitoring and assessment.

The currently accepted standard for the conduct of clinical trials requires that three main parameters be fulfilled. Subjects should be randomly assigned to treatment groups; the person conducting the assessment of the outcome measure should be blinded to the treatment being given; and the treatment being tested should be compared with either an established treatment, no treatment, or a placebo. Although the first two design features can easily be incorporated into trials of homeopathy, the third poses considerable problems. Placebo-controlled trials are often considered poorly suited to the evaluation of homeopathy (Weatherley-Jones and others 2004) because practitioners claim it is not unusual to have to try two or three remedies before identifying one that is efficacious. Also, the optimal remedy may change with time as the patient's signs alter. The question asked by homeopathic practitioners is 'What should be done at a second consultation if the patient has not responded, but it is not known whether the patient has received the remedy or the placebo?' Comparing the first remedy that is selected with a placebo is therefore likely to underestimate the potential of the homeopathic approach.

The aim in this pilot study was to use conventional methods of diagnostic investigation in cases of atopic dermatitis in dogs, and then to monitor the response to remedies prescribed according to homeopathic principles. In an attempt to address some of the complexities outlined above, a novel, two-stage study design was tested in order to allow adherence to both homeopathic and allopathic principles. In phase 1, the aim was to identify dogs that showed an apparently positive response to homeopathic remedies; in phase 2, the responding dogs were put forward into a randomised, blinded, placebo-controlled phase to see whether that response could be linked to a homeopathic remedy. The results from this study were intended to be used to inform the design of a larger randomised controlled trial, including the potential for using placebos.

TABLE 1: Age, breed and sex of the dogs included in the study

Dog	Age of enrolment	Breed	Sex
1	1 year, 5 months	Crossbreed	FN
2	1 year, 6 months	Golden retriever	F
3	2 years, 7 months	Soft coated wheaten terrier	MN
4	1 year, 6 months	Labrador retriever	M
5	1 year, 1 month	Jack Russell terrier	M
6	2 years, 5 months	English setter	MN
7	3 years	Border terrier	MN
8	5 years, 7 months	West Highland white terrier	MN
9	4 years, 7 months	Labrador retriever	FN
10	6 years, 6 months	German shepherd dog	F
11	2 years	Jack Russell terrier	FN
12	4 years, 1 month	German shepherd dog	FN
13	1 year, 6 months	Boxer	FN
14	2 years, 8 months	Border terrier	MN
15	7 years	English bull terrier	FN
16	2 years	Staffordshire bull terrier	FN
17	2 years, 7 months	Golden retriever	FN
18	3 years, 6 months	Staffordshire bull terrier	M
19	2 years	Cairn terrier	MN
20	5 years	Lhasa apso	M

F Female, FN Female neutered, M Male, MN Male neutered

Materials and methods

Dogs

Twenty dogs were recruited to the study from the dogs referred to the dermatology clinic at the University of Bristol School of Veterinary Science. Details of the dogs' age, breed and sex are shown in Table 1. The median age at recruitment was two years and seven months.

Diagnostic inclusion criteria

Dogs were diagnosed with non-seasonal atopic dermatitis if they had a history and clinical signs consistent with published criteria (Willemse 1986, Prélaud and others 1998, DeBoer and Hillier 2001, Griffin and DeBoer 2001). Pruritus due to ectoparasites, infectious agents or dietary intolerances was ruled out or controlled before the dogs entered the study. Ectoparasitic dermatoses were excluded by performing skin scrapings and hair pluckings and observing the response to treatments with appropriate antiparasitic agents. Pruritus due to staphylococcal infection was excluded if typical lesions were not present, or was treated with appropriate antimicrobial therapy before the dogs entered the study. *Malassezia* species overgrowth was detected using stained acetate tape strips. Adverse reactions to food were ruled out as completely as possible, depending on the owners' compliance; in any study of this kind, there is a possibility that some dogs with a concurrent dietary intolerance may have remained in the study group.

The dogs underwent intradermal allergy testing using a panel of 40 allergens (12 dogs) or had serum submitted for IgE serology (one dog), or had both tests performed (seven dogs). Positive skin test reactions were identified subjectively using standard criteria (Hillier and DeBoer 2001). All the dogs entering the study had positive reactions to multiple allergens, confirming the diagnosis of atopic dermatitis.

Participation

Participation in the study was voluntary. All the owners of dogs diagnosed with atopic dermatitis were invited to take part, but only some agreed. The reasons for not taking part included the dog having severe

disease, a desire to start conventional treatment, reluctance to consider homeopathy, inability to return for necessary rechecks or general uncertainty about clinical trials.

TABLE 2: Rubrics (signs) used by the veterinary homeopath to select remedies*. The rubrics were identified by questioning the owner and examining the dog. Local signs included clinical signs associated with the skin or other organs. Constitutional signs included personality or character traits, or a history of the skin problem commencing shortly after vaccination. Where more than one remedy is listed, the subsequent remedies were prescribed at follow-up consultations, not given concurrently

Dog	Local signs	Constitutional signs	First remedy	Subsequent remedies
1	Pruritic feet, anus, ears	Vaccinosis	Sulphur 30C	Pulsatilla 200C
2	Pruritic ventrum, groin, axillae Pustules Hyperpigmentation	None	Arsenicum iodide 30C	
3	Pruritic distal forelimbs and metatarsals Erythema Lichenification Multifocal alopecia Crusts Hyperpigmentation Right-sided otitis	Likes to be cool Likes routine	Pulsatilla 200C	Kali sulph 30C
4	Generalised pruritus Wet eczema on rump Hyperpigmentation of the ventrum Heat	Enthusiastic Stubborn Aversion to onions	Sulphur 30C	Pulsatilla 30C
5	Pruritus Ataxia Seizures	Jealous Inquisitive	Lachesis 30C	Sulphur 30C Morgan 30C
6	Pruritus Worse when warm and damp	Over-affectionate Desires music Desires activity	Carcinosin 200C	Silicea 30C
7	Pruritus axillae and groin Vomiting and bloody diarrhoea at night	Affectionate Jealous Likes routine	Arsenicum album 200C	Sulphur 30C Kali sulph 30C
8	Pruritus under tail, hindlimbs and chin	Jealous Sensitive to noise Avoids puddles Enjoys open air	Pulsatilla 200C	
9	Pruritic perineum and chin	Jealous Prefers cool Dislikes rain	Pulsatilla 200C	
10	Pruritic face, axillae, groin Right-sided blue/black skin discoloration	Fear of thunder and noise Dislikes cold and wet Desires cheese	Sulphur 30C	Phosphorus 30C Phosphorus 200C Sepia 30C
11	Pruritic face, flanks, feet No eruption False pregnancies	Jealous Dislikes milk Likes warm not heat Dislikes wet Very sensitive but does not console owner	Pulsatilla 200C	Arsenicum iodide 30C and 1M

Concurrent medications

Concurrent conventional medications were permitted during the study if the dog was on long-standing medication for a non-dermatological condition, or was currently receiving conventional medication for its skin condition and sudden withdrawal of that medication would not be in the animal's best interests. This category included dogs that had residual, stable and persistent pruritus despite receiving glucocorticoids, ciclosporin or allergen-specific immunotherapy. In the case of allergen-specific immunotherapy, the dog must have been receiving the treatment for at least nine months so that further improvements were not to be expected. Vaccinations were not permitted during the study period.

To improve compliance with the study, the owners were given a supply of prednisolone tablets in case there was a sudden worsening of their dog's signs of pruritus. The owners were told that they should administer these tablets only on the advice of one of the dermatologists, or if, in their opinion, the pruritus was worsening significantly at a time when a dermatologist was not available.

Withdrawal criteria

Withdrawal criteria during the study period included poor owner compliance, an unacceptable level of discomfort for the dog in the opinion of the owner or veterinary surgeon, or the requirement for additional conventional treatments to be prescribed during the treatment period.

Clinical assessment

The severity of pruritus was used as the single outcome measure in this study. Pruritus was assessed by the dogs' owners using a validated and published anchored visual analogue scale, which has severity, frequency and behavioural factors embedded within it (Hill and others 2007). As this pilot study aimed only to determine the effect of the remedies on the level of pruritus, concurrent assessment of lesion scores with a CADESI (Canine Atopic Dermatitis Extent and Severity Index) scale (Olivry and others 2007) was not performed. In order to justify consideration of a future, larger, randomised controlled trial, at least 25 per cent of the dogs were required to have shown a satisfactory reduction in their pruritus scores by the end of their period of investigation. For dogs with initially high pruritus scores (at least 5·0), this degree of improvement was defined as a score reduction of at least 50 per cent, whereas for dogs with initially lower scores (less than 5·0), a decrease to a score less than 2·5 was required.

Homeopathic consultation

After agreeing to participate in the study, the owners attended a consultation conducted by a veterinary homeopath (JH), with one of the dermatologists (PH, PL-G or JR) in attendance. During the consultation, the owners were asked a series of questions relating to the dog's skin problem, general health and personality traits, and the dog's skin was examined. Based on the responses and clinical findings, the signs and features of the case (known as rubrics) were entered into a homeopathic software programme used to identify appropriate remedies (MacRepertory – the Complete 2005 Repertory; Kent Homeopathic Associates). Remedies that matched closely with the documented signs were scrutinised, and if a single remedy did not emerge as the optimal candidate, a final choice was determined by the homeopath based on clinical experience. The individualised remedies were then prescribed and the owner was instructed to administer them by crushing the tablets and tipping the powder into the dog's mouth so that it contacted the buccal mucosa.

Study protocol

Open phase Owners of dogs participating in the study were requested to attend the clinic on day 0 (the initial homeopathic consultation) and 30 and 60 days later. After day 60, an owner could continue to bring the dog for further homeopathic consultations on a monthly basis if they wished to pursue this type of treatment for a longer period.

At each visit, the dog's pruritus score was recorded and the skin was examined. At each consultation after day 0, the owners were given the following options, depending on the response that had been observed: if the pruritus had completely resolved, the dog could be withdrawn from the study and monitored for future relapses; if the pruritus had not completely resolved, but had decreased to a level that the owner considered a beneficial response, further remedies could be prescribed (either the same or modified); if the pruritus level had not decreased, the owner was

TABLE 2: Continued

Dog	Local signs	Constitutional signs	First remedy	Subsequent remedies
12	Pruritus No eruption Mainly left side Fissures on lips Delayed first oestrus	Aggravated by milk, fats, rich food Jealous Affectionate Indignation	Pulsatilla 200C	Natrum mur 200C
13	Pruritic axillae, chest, groin, ears Aggravated by rubbing	Desires fish, milk Sleeps with head low Jealous Vaccinosis?	Sulphur 30C	Sulphur 200C Kali carb 30C
14	Pruritus Heat	Eats anything, including animal faeces Rolls in faeces Jealous Stubborn No fears	Sulphur 30C	Arsenicum iodide 30C and 1M Sulphur 200C
15	Pruritic feet, ventrum and axillae Aggravated by rich food Loud flatus when excited	Dislikes rain and getting feet wet Likes fuss Does not scratch when on owner's lap Loves children Lies on back with feet in air	Pulsatilla 200C	
16	Pruritic feet Will scratch until skin raw Arthritic swellings left elbow	Affectionate Fears thunderstorms Clairvoyant Grief Desires chicken; oranges aggravate	Phosphorus 200C	Aconite 1M Atopica 200C Phosphorus 200C Carcinosin 200C
17	Pruritus, axillae and groin, worse in morning Pustules in groin Discharge of black wax from ear Ravenous appetite	Better for cold Likes cold bathing Fear of men Jealous Lesions worse on right side of body	Sepia 200C	Sulphur 30C Staphisagria 200C Sulphur 200C Pulsatilla 200C Pulsatilla 1M
18	Pruritus, belly and nipples Erythema and lichenification Seeks sun but warmth aggravates	Hates thunder and noise Spices/rich food causes diarrhoea Inquisitive Anticipates owner's actions Consoles the sick	Phosphorus 200C Atopica 200C	
19	Pruritus, inguinal region and all feet	Very sensitive to noise Gentle Cold bathing ameliorates Will eat anything ravenously except garlic	Natrum mur 200C	Natrum mur 1M Arsenicum album 30C
20	Pruritus, inguinal area and all feet Pustules present	Gentle Likes routine Warmth aggravates	Pulsatilla 200C	Sulphur 30C

* Homeopathic prescribing is based on a peculiar form of notation used within the repertory. For example, an itching wrist is translated into the rubric of 'Extremities, itching, upper limbs, wrists'; avoiding puddles becomes 'Extremities, wetting, feet, aggravates.' For the purposes of this table, standard English terminology has been used, and the categories within the repertory known as Mental and General signs are listed together as Constitutional signs. The letters C and M refer respectively to the centesimal and millesimal potencies of homeopathic dilution (that is, 30C is a 1:100 solution that has been serially diluted 30 times)

given the option of either changing the remedy (if an alternative was thought to be appropriate) or withdrawing from the study and reverting to conventional therapy.

Blinded, randomised, placebo-controlled phase If owners considered that there had been a substantial response to a homeopathic remedy prescribed during the open phase (defined as a reduction in the dog's pruritus score of 50 per cent or more), they were invited to take part in a follow-up, blinded, randomised, placebo-controlled phase. The aim of this phase was to determine whether the responses reported to the homeopathic remedy could be distinguished from responses to a placebo (simple lactose tablets, the vehicle pill used for all the homeopathic remedies). For this phase, owners were given two vials of pills, labelled X and Y, one containing the remedy and one containing the placebo. The owners were blinded to the content of the vials, and the order in which the tablets were administered was randomised using an online random number generator (Research Randomizer 2008). The owners were asked to give the pills labelled X first and to score the level of pruritus seven days later. The pills labelled Y were given two weeks after those labelled X if the dog was still pruritic, or whenever pruritus recurred.

Statistical analysis

The responses to treatment were analysed by intention-to-treat analysis, that is, the final pruritus scores for any dogs that were withdrawn during the study would be used for the final analysis. Changes in the pruritus scores over time were analysed by Friedman's repeated measures analysis of variance, with individual time points compared by Dunn's post hoc comparison.

Results

Clinical features at the time of enrolment

The mean duration of pruritic skin disease before the dogs entered the trial was 26 months (range seven to 72 months). The pruritus scores ranged from 3·5 to 8·0, with a median of 6·55. The number of allergens identified by skin testing and/or IgE serology ranged from two to 19.

Rubrics and remedies

The rubrics and remedies for each dog are summarised in Table 2. Sixteen different homeopathic remedies were prescribed throughout the course of the study. The most commonly prescribed remedy at the first consultation was Pulsatilla 200C (given to seven dogs), followed by Sulphur 30C (five dogs). Phosphorus 200C was given to two dogs, and single dogs were treated with Arsenicum iodide 30C, Lachesis 30C, Carcinosin 200C, Arsenicum album 200C, Sepia 200C and Natrum mur 200C. All dogs were treated with a single remedy apart from one dog, which was receiving conventional ciclosporin when it entered the study. This dog was given homeopathic ciclosporin (Atopica) 200C at the same time as Phosphorus 200C.

Fifteen dogs were given a different remedy at the second or subsequent consultations, either because the first remedy had not shown any effect, or because the presenting signs had changed. Remedies prescribed at follow-up visits that had not been used in the primary consultation included Kali sulph 30C, Kali carb 30C, Pulsatilla 30C, Pulsatilla 1M, Morgan 30C, Silicea 30C, Phosphorus 30C, Sepia 30C, Aconite 1M and Staphisagria 200C.

All the remedies were administered as either a split dose (three pills given over a 24-hour period) or twice daily doses for up to five days. In some cases, depending on the remedy, its potency and the response seen by the owner, a second course was administered after a gap of five to 14 days. No remedies were administered on a continuous daily basis.

Clinical responses

Open phase All 20 dogs were evaluated on days 0 and 30; 19 dogs were evaluated on day 60. One dog did not attend on day 60, but was scored on day 150. For this dog, the day 150 score was used both for the final analysis and for the analysis of day 60 scores. Fourteen owners elected to continue with the study until day 90, eight continued until day 120, five continued until day 150, one continued until day 180 and one continued until day 210. No cases were withdrawn from the study due to poor owner compliance or following the administration of conventional medications.

TABLE 3: Pruritus scores of the 20 dogs throughout the trial, and changes in score between day 0 and the end of each dog's participation in the study. The dogs have been ranked in order of greatest to least percentage improvement. Scores were provided by owners using a validated anchored visual analogue scale from 0 to 10. The first homeopathic consultation took place on day 0.

	Day								
Dog	0	30	60	90	120	150	180	210	Change of score (%)
6	3·5	2·1	0	0	0				–3·5 (–100)
15	7·5	10	4·3	0·8					–6·7 (–89)
12	8·4	5·4	4·6	4·2	2·3	1·6			–6·8 (–81)
4	7·7	6·8	2·6	2·3					–5·4 (–70)
9	8·0	7·5	3·1	2·9					–5·1 (–64)
13	7·8	9·9	4·3	4·3					–3·5 (–45)
2	6·3	3·4	4·6						–1·7 (–27)
18	6·2	7·4	5·9	5·4					–0·8 (–13)
17	3·8	3·3	4·2	4·4	3·5				–0·3 (–8)
5	7·7	7·2	7·2						–0·5 (–7)
1	6·5	6·5	6·2						–0·3 (–5)
14	6·5	5·9	4·0	3·9	4·0	4·1	4·3	6·2	–0·3 (–5)
7	7·5	8·2	6·7	7·3	7·2	7·2			–0·3 (–4)
20	6·6	6·0	6·5						–0·1 (–2)
16	6·8	6·7	6·0	6·7	7·0				0·2 (+3)
19	5·8	7·0	7·9	6·2					0·4 (+7)
3	7·6	6·4	8·2						0·6 (+8)
10	5·0	4·4	4·3	5·8	5·6				0·6 (+12)
11	4·4	4·1	4·4	7·3	2·2	4·3	2·4	5·2	0·8 (+18)
8	5·3	1·2				8·0			2·7 (+50)
Median	6·55	6·45	4·6	4·35	3·75	4·3	3·35	5·7	

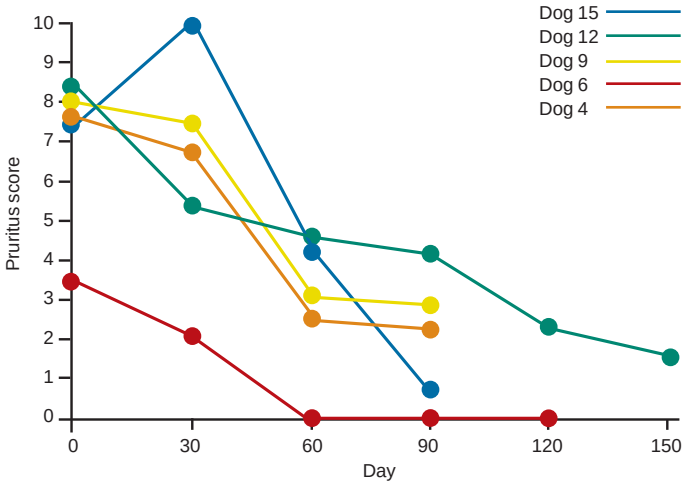

FIG 1: Pruritus scores of five dogs that showed a good response to homeopathic remedies. The initial homeopathic consultation took place on Day 0. Dog 6 had been receiving allergen-specific immunotherapy and 30 mg prednisolone per month for over a year before entering the study, but these treatments were discontinued by day 60. Dog 15 was receiving 5 to 10 mg prednisolone per day on day 0, but this was reduced to 2·5 mg prednisolone every other day by day 90. Dogs 4, 9 and 12 had received intermittent glucocorticoids for two to four years before entering the study, but no glucocorticoids were given during the study period

The pruritus scores of the 20 dogs throughout the study are shown in Table 3. The scores varied widely, both on a group basis and for individual dogs. The pruritus scores on day 60 were significantly lower than on day 0 (Friedman's repeated measures analysis of variance with Dunn's post hoc comparison; P=0·0127). Fourteen dogs had lower pruritus scores at the end of the study than the beginning, and six dogs had higher scores at the end of the study. Five of the dogs had a decrease in pruritus score of at least 50 per cent (Fig 1); these dogs were selected for the second phase of the study.

Blinded, randomised, placebo-controlled phase The owners of dog 6 did not participate in the second phase of the trial because the dog's clinical signs resolved and it did not require further medication. Dog 15 did not participate because it was euthanased shortly after concluding the first phase of the study when it suffered status epilepticus; this dog had suffered seizures throughout its life and was receiving phenobarbital. The remaining three dogs continued to receive homeopathic remedies on an intermittent basis and could therefore be given either the remedy or placebo, as described above.

The owner of dog 12 reported a 0·2 point reduction in the dog's pruritus score following placebo treatment and a 2·4 point reduction following treatment with the remedy. The owner of dog 4 reported no change following the placebo and a 4·3 point reduction in pruritus score following the remedy. The owner of dog 9 reported a 0·8 point reduction in pruritus score following the placebo and a 3·0 point reduction following the active remedy.

Discussion

To the authors' knowledge, this is the first study in small animal veterinary medicine to combine conventional diagnostic approaches with individualised homeopathic prescribing. The aim was to design a pilot study to generate data that could be interpreted by both homeopathic practitioners and conventional veterinary clinicians, and that could be used to inform the design of a larger randomised controlled trial.

The design of the study was unusual in that only dogs that apparently showed a substantial response to the initial treatment were put forward to a randomised controlled phase. This departure from a standard clinical trial design, in which blinding, randomisation and a control group would be used from the outset, was examined for a number of reasons. First, the authors wanted to allow true homeopathic prescribing principles to be used, which may entail a number of changes of remedy before an optimal treatment is established. Second, the time taken to effect a clinical response may be longer with homeopathic remedies than with conventional drugs, and the authors wanted to allow a degree of flexibility so that this phenomenon could be accommodated. Third, the dermatologists wanted to observe the progress of the dogs in an open study, so that they could gain a greater understanding of the likely outcomes in a typical clinical setting. Finally, this was a pilot study, and it is not unusual for open clinical trials to report preliminary data that can be used subsequently to justify larger randomised trials. The performance of an open pilot study is indispensable to allow a power analysis before a randomised controlled trial, and to enable the study design and choice of controls to be modified on the basis of the effect of the drug being tested. This approach was adopted during the introduction of ciclosporin as a treatment for canine atopic dermatitis (Fontaine and Olivry 2001, Olivry and others 2002a, b, Steffan and others 2003).

The addition of a blinded, randomised, placebo-controlled crossover phase to investigate dogs that showed a substantial improvement in the open phase was designed as one possible way to legitimise any such responses according to conventional criteria. Although this phase satisfied conventional criteria for good clinical trial design, the authors were not aware at the outset how many dogs might progress to this stage. In addition, a problem predicted by the homeopath in advance was that some dogs might undergo complete resolution of their clinical signs and thus not be eligible for further investigation. Homeopathic practitioners aspire to cure patients of their clinical signs by encouraging their bodies to heal and only a proportion of patients need to be given regular medications. However, in relation to the management of canine atopic dermatitis, the authors believed that the identification of a subgroup of dogs that, in the opinion of their owners, responded well to the intermittent administration of remedies, would be most likely to yield answers about the effectiveness of homeopathy in the management of the disease.

The results of the study are likely to provoke debate from both homeopathic and conventional veterinary practitioners. Homeopathic practitioners may interpret the results as providing evidence that the prescribed remedies were effective in 25 per cent or more of the dogs included in the study. The magnitude of these clinical responses (between 64 and 100 per cent improvement in the pruritus scores of five dogs, with a smaller improvement in another nine dogs), together with the ability of the owners of the three dogs that completed the second

phase to distinguish correctly between a placebo and an active remedy, would strengthen the argument for this view.

Conventional clinicians who are sceptical about homeopathy might interpret the results differently, and attribute the responses to chance and 'wishful thinking' on behalf of the owners. Seventy-five per cent of the dogs showed clinically insignificant responses or deterioration in response to the homeopathic treatment, and any mild improvements noted could have been due to natural waxing and waning of their condition. However, a sceptical analysis of the five dogs that showed what appeared to be a good response to the remedies is more problematic. One dog's skin condition resolved completely following homeopathic treatment, allowing the discontinuation of conventional treatments (immunotherapy and glucocorticoids) that it had received for two years. Although spontaneous resolution could be proposed as the explanation for this improvement, canine atopic dermatitis is regarded as an incurable disease requiring lifelong management (Scott and others 2001), and the chances of a sudden resolution occurring coincidentally after the remedies had been administered would be small. The owners of another three dogs correctly distinguished between a homeopathic remedy and a placebo pill. A sceptical interpretation might put this down to chance, although the probability of it occurring randomly is only 12·5 per cent.

The authors' interpretation of the results is that they provide data to justify a larger study to determine whether the findings are repeatable. Although there was a significant reduction in pruritus scores between days 0 and 60 when all the dogs were considered together, the changes seen in three-quarters of the dogs were not clinically relevant. The mild to moderate fluctuations in pruritus score could have occurred due to well known phenomena such as regression to the mean or waxing and waning of disease severity, but it was impossible to assess this without the inclusion of an untreated control group for comparison. However, the sustained beneficial response seen in five of the dogs clearly warrants further investigation. Before entering the study, these dogs had been receiving various conventional medications, including glucocorticoids, for between one and six years in an attempt to control their atopic dermatitis. Dogs 6 and 9 had been assessed by specialist veterinary dermatologists in the past and their clinical signs were not considered by their owners to be under satisfactory control, despite the dogs receiving ongoing medication. The owners of the five dogs were in no doubt that the improvements seen in their dogs' signs were a result of the homeopathic remedies. One further owner (of dog 2) believed that a significant improvement had occurred in the dog, even though a reduction in pruritus score of only 27 per cent was obtained during the formal trial period. This dog was not put forward to the placebo-controlled phase, but subsequent telephone follow-up indicated that the dog went into remission and no longer required conventional treatment. Furthermore, according to the owner, a minor flare-up occurring several months later responded promptly to a repeat dose of the original homeopathic remedy.

In a study such as this, a consideration of the failure rate is required as well as of the potential successes. The success rate was lower than the 60 to 70 per cent predicted by the homeopath at the outset of the study. There are four potential explanations for this discrepancy. First, the group of dogs studied was derived from a referral population. These cases are typically more severe than those seen in general practice, and many require potent drugs or complex treatment regimens to keep them in remission. Furthermore, recruitment of cases on to the study was voluntary, and owners appeared more eager to participate if they had already exhausted a number of other treatment options; thus, a group of dogs that was particularly difficult to manage may have been selected. Secondly, many of the dogs had received, or were receiving, glucocorticoids or ciclosporin. Homeopaths believe that these immunosuppressive drugs can interfere with the action of homeopathic remedies. Thirdly, the anticipated success rate when treating canine atopic dermatitis with homeopathic remedies may have been based on previous clinical impression, rather than recorded data, and the response rates obtained in this study may represent the true outcomes that can be expected. Fourthly, if the beneficial responses were due to spontaneous recoveries and chance occurrence, the failure rate would merely reflect the fact that homeopathy is not an effective treatment for canine atopic dermatitis.

Although these factors need to be borne in mind when designing future studies, the authors consider that the overall success or failure rate in this study is somewhat irrelevant. The objective of this study was to determine whether homeopathic remedies appeared to be beneficial in enough cases of canine atopic dermatitis to justify a larger trial. Even with a cautious interpretation, the preliminary data appear to support that view, and the authors believe that a large randomised and controlled trial is required to confirm or refute the findings. If a similar balance of responders and non-responders were obtained in the future, it is likely that the trial would need to be performed at several centres in order to recruit enough dogs.

One final point that must be emphasised is that this study has looked at one sign (pruritus) of one disease (atopic dermatitis) in one species (dogs), and readers are urged not to make inferences about homeopathy in general. There is no justification for using the findings reported here to substantiate or repudiate the overall efficacy of homeopathy in either veterinary or human medicine.

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