A blinded, placebo-controlled study of the efficacy of borage seed oil and fish oil in the management of canine atopy

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Twenty-one dogs with atopy were entered into a blinded, placebo-controlled study lasting eight weeks. They were randomly divided into three groups and were all given supplementary oils orally once daily. The dogs in groups A and B were given borage seed oil and fish oil in combination (Viacutan; Boehringer Ingelheim Vetmedica) to provide 176 mg/kg or 88 mg/kg borage seed oil respectively. The dogs in group C were given 204 mg/kg olive oil as a placebo. They were all re-examined after four and eight weeks and scored for pruritus, erythema, oedema, alopecia and self-excoriation. After eight weeks the scores for erythema and self-excoriation, and the total score for the dogs in group A, and the total score for the dogs in group B were significantly reduced (P<0·05). The dogs in group C showed no significant improvement.

THE efficacy of essential fatty acids in the treatment of canine atopy has been reported in several blinded studies. Bond and Lloyd (1992a, b) and Scarff and Lloyd (1992) used supplements predominantly of evening primrose oil and Logas and Kunkle (1994) used marine fish oil, and showed that they helped to suppress the clinical signs in some dogs with atopy.

The beneficial effect of supplements of essential fatty acids is thought to be due principally to their influence in balancing pro- and anti-inflammatory mediators (Nassar and others 1986a, b, Ziboh and Chapkin 1988, Miller and others 1991, Horrobin 1993). Thus gamma-linolenic acid (18:3n6) acts as a precursor for 1-series prostaglandins and other metabolites which are less inflammatory, or even anti-inflammatory, compared with 2-series prostaglandins (Ziboh and Chapkin 1988). Linoleic acid (18:2n6) may also play a beneficial role because in addition to acting as a substrate for the biosynthesis of eicosanoids, it is an important component of biological membranes (Murphy 1990). The configuration and function of membrane-bound and transmembrane receptors and enzymes is affected by the fluidity of the phospholipid cell membrane, and cellular function may therefore be affected by the balance of essential fatty acids within the constituent phospholipids (Engelhard and others 1976, Traill and Wick 1984). Furthermore linoleic acid is important for the correct disposition and function of the epidermal barrier to permeability, which is composed predominantly of lipid bilayers (Bowser and others 1985).

Borage seed oil contains roughly twice the concentration of gamma-linolenic acid, and very much less linoleic acid than evening primrose oil (Horrobin and Manku 1990). However, the absolute concentration of the putative anti-inflammatory fatty acid within a given oil is not the only factor to be considered when selecting a supplement. For example, the presence and position of other fatty acids on the triglyceride molecule will influence its rate of hydrolysis by pancreatic lipases, and therefore the biological availability (Litchfield 1972, Lawson and Hughes 1988).

Borage seed oil contains approximately 19 per cent of gamma-linolenic acid (Horrobin and Manku 1990) and stereochemical factors suggest that it should be biologically available and presumably, therefore, of therapeutic value. This suggestion has been supported by experimental studies which have demonstrated that oral doses of borage seed oil can influence the metabolism of essential fatty acids in a manner consistent with anti-inflammatory activity (Miller and others 1990, 1991, Pullman-Mooar and others 1990) and by clinical studies demonstrating a therapeutic effect in man (Landi 1993).

This paper describes the results of a double-blinded trial of a combination of borage seed and fish oils as a source of essential fatty acids for the treatment of canine atopy, using olive oil as a placebo control.

MATERIALS AND METHODS

Dogs with atopy diagnosed on the basis of the criteria outlined by Willemse (1986), were screened for dietary intolerance by the feeding of a novel diet for at least six weeks. When they were diagnosed, the options for management of the disease were explained to the owners and they were offered a place on the trial. A final decision on the institution of specific therapy, for example immunotherapy, was deferred until after the trail. Dogs with secondary pyoderma or *Malassezia pachydermatis* dermatitis, both of which increase pruritus and neither of which is responsive to essential fatty acids, were excluded.

Twenty-one dogs were selected on the basis of the above criteria and were allocated at random to one of three groups. They were all given gelatine capsules which contained either a mixture of borage seed oil and fish oil, olive oil alone or a mixture of all three. In order to blind the study, the capsules were provided in two boxes (1 and 2). The owners were instructed to administer two capsules from each box per 10 kg bodyweight. For the dogs in group A both boxes contained the borage/fish oil mixture whereas for group C both boxes contained olive oil. For the dogs in Group B, one box contained borage/fish oil, the other, olive oil. The actual intakes of oils and the amounts of essential fatty acids received by each group are given in Table 1.

The author was unaware of the treatment being given until the trial was closed and the codes broken. The dogs were weighed and scored for pruritus (owner's assessment, based on knowledge of previous scores), the degree of erythema (particularly the plantar and dorsal interdigitae, the concave aspect of the pinna and the verticular ear canal), interdigital oedema, alopecia and self-excoriation. The individual scores were marked out of 10 and a total score was calculated as the sum of the scores, when the dogs entered the trial, and when they were re-examined after four and eight weeks of treatment. At the close of the study the owners' compliance was checked by comparing the numbers of capsules used with the numbers which should have been used.

The scores for pruritus, erythema, oedema, alopecia and self-excoriation, and the total scores for the three groups were compared by Mann Whitney non-parametric tests, using a commercial statistical package (Minitab for Windows; Minitab Inc), with any differences being considered significant at P<0·05.

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TABLE 1: Daily doses (mg/kg) of the various oil combinations given to the dogs in groups A, B and C

Group	Borage oil	Fish oil concentrate	Olive oil	GLA	EPA	DHA	Total daily supplement
A	176	22	–	42	4·2	2·7	198
B	88	11	102	21	2·1	1·3	201
C	–	–	204	–	–	–	204

GLA Gamma-linolenic acid 18:3n6, EPA Eicosapentaenoic acid 20:5n3, DHA Docosahexaenoic acid 22:6n3

TABLE 2: Summary of the results for the 18 dogs which finished the trial

	Pruritus week			Erythema week			Oedema week			Alopecia week			Self trauma week			Total week		
Group A	0	4	8	0	4	8	0	4	8	0	4	8	0	4	8	0	4	8
1	4	3	2	4	2	0	0	0	0	0	0	0	1	0	0	9	5	2
2	6	4	4	5	1	1	2	0	0	4	2	2	5	1	1	22	8	8
3	5	5	5	4	4	4	3	3	3	5	5	5	4	4	4	21	21	21
4	4	4	2	3	0	0	1	0	0	0	0	0	2	0	0	10	4	2
5	6	7	4	7	6	2	3	3	1	3	1	1	5	4	0	24	21	8
6	5	4	4	6	4	4	1	0	0	0	0	0	2	0	2	14	8	10
Total	30	27	21	29	17	11*	10	6	4	12	8	8	19	9	7*	100	67	51*
Group B																		
1	3	3	4	5	2	5	1	0	0	2	0	0	3	0	0	14	5	9
2	5	6	4	6	5	3	2	2	0	0	0	0	5	5	2	18	18	9
3	4	2	1	2	0	0	0	0	0	3	3	1	0	0	0	9	5	2
4	4	3	2	4	0	0	1	0	0	0	0	0	0	0	0	9	3	2
5	4	3	2	3	1	0	1	0	0	0	0	1	3	0	1	11	4	4
Total	20	17	13	20	8	8	5	2	0	5	3	2	11	5	3	61	35	26*
Group C																		
1	4	3	4	3	0	4	2	0	1	1	0	0	3	0	3	13	3	12
2	7	7	4	4	5	2	1	0	0	0	0	0	2	4	2	14	16	8
3	3	3	3	4	0	4	0	0	0	0	0	0	3	0	3	10	3	10
4	5	4	4	6	4	4	2	2	2	0	0	0	2	1	3	15	11	13
5	4	6	6	5	7	5	1	2	2	0	0	0	2	3	3	12	18	16
6	3	3	1	3	2	0	1	0	0	0	0	0	1	0	0	8	5	1
7	5	5	5	4	4	4	1	1	1	2	2	2	4	4	4	16	16	16
Total	31	31	27	29	22	23	8	5	6	3	2	2	17	12	18	88	72	76

* Significant reduction

RESULTS

Eighteen of the 21 dogs completed the study. One dog in group A was withdrawn after five weeks because it contracted scabies, and one dog in group C, and one dog in group B were withdrawn after six weeks because they failed to respond. There were six dogs in group A, five in group B and seven in group C (Table 2). None of them showed side-effects during the course of the trial.

The dogs in group A showed a significant ($P<0·05$) decrease in erythema and self-trauma during the eight weeks, and their total score was also significantly decreased (Table 2). The dogs in group B showed a significant improvement in total score ($P<0·05$) but although most of the individual parameters were improved with treatment none reached statistical significance (Table 2). The dogs in Group C showed no significant improvement (Table 2).

DISCUSSION

It is difficult to assess the effect of essential fatty acids, or indeed any anti-inflammatory agent, in the management of canine atopy because of the fluctuating nature of the dermatosis. Seasonal fluctuations in the concentration of allergens, secondary infections with staphylococci and malassezial yeasts, and xerosis may affect the pruritus and other clinical signs displayed by atopic dogs and influence their therapeutic requirements (Bond and Lloyd 1994). Every effort was made to minimise or nullify these factors by excluding dogs with secondary infections from the study, and by using parallel cohorts to exclude a seasonal bias.

Although the author was blinded to the nature of the supplement until the study ended, astute owners could have been aware that they were in group B, because their dogs were given a mixture of capsules. However, the owners of dogs in groups A and C could not have been aware of the treatment given to their dogs. Whether the owners of dogs in group B did in fact draw any conclusions about their dogs' medication and whether this influenced their reporting of pruritus, for example, is not known.

The results support the contention that a mixture of borage seed oil and fish oil has the potential for good anti-inflammatory activity in the management of canine atopy. Dogs treated with essential fatty acids derived from evening primrose oil or fish oil, have been reported to require treatment for six to 12 weeks before the improvement maximises (Bond and Lloyd 1994, Logas and Kunkle 1994), although a recent blinded study by Scott and others (1997) reported maximal responses within one to three weeks. The dogs in groups A and B were treated for eight weeks before a significant improvement was observed although there was some improvement after four weeks. Bond and Lloyd (1994) reported that the effects of supplementation with evening primrose oil appeared to be dose-responsive. The greater improvement observed in the dogs of group A in this trial also suggests that the effects were dose-responsive.

The period of perhaps six to 12 weeks before maximal effects are observed (Bond and Lloyd 1994, Logas and Kunkle 1994), suggests that further improvements might have been obtained in groups A and B if the study had been continued. However, it is considered unlikely that the dogs in group C would have improved, given their failure to show any improvement over the eight weeks of the study.

Some of the dogs in both groups A and B failed to respond as well as the others. The fact that certain individuals, or breeds, appear to be refractory to supplementation with essential fatty acids was reported by Bond and Lloyd (1994) and Scott and others (1997). In one study, the differences in the responses to evening primrose oil supplementation in people were ascribed to differences in their overall dietary oil intake (Biagi and others 1988). Scott and others (1997) reported results which appeared to indicate that there might be biochemical differences between the dogs which responded to supplements of essential fatty acids and those which did not. In this study no effort was made to feed all the dogs the same diet. Although the random nature of the study should have reduced any dietary effects it is possible that the essential fatty acid content of the dogs' diets may have affected the results, because the concentrations in commercial foods vary greatly (Scott and others 1997). Other factors which may affect the responses of individual dogs include subtle differences in the disease that may not be detected clinically, and differences in the pruritic threshold of individual dogs.

The effect of fish oil in the supplements is unknown, although it may have been beneficial (Scott and Miller 1991, Logas and Kunkle 1994). More work is needed to investigate the relative effects either of n:6 or n:3 essential fatty acids, and whether mixtures of the two are superior in the management of atopy (Campbell 1993). However, this study has demonstrated that the high concentration of gamma-linolenic acid in borage seed oil, in combination with fish oil, does appear to possess an anti-inflammatory action.

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Spinal cord injury in small animals 1. Mechanisms of spontaneous recovery

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Spinal cord injury causes obvious clinical deficits early in the course of lesion evolution, but it is commonly observed that recovery can occur spontaneously during a period of days, weeks or even months afterwards. Spinal cord dysfunction arises after injury because of a combination of reversible alterations in the concentration of intra- and extracellular ionic constituents and irreversible tissue destruction. Recovery can therefore occur through re-establishment of the normal microenvironment of the spinal cord, which occurs soon after injury induction, and also by formation of new patterns of central nervous system circuitry. Alterations in circuitry, termed 'plasticity', can occur during the immediate period after injury but apparently continue for many weeks or months. There are differences in the extent and nature of recovery between complete and incomplete experimental spinal cord injuries that illustrate the roles played by reorganisation of intra- and suprasegmental circuitry. Information that is available on mechanisms of spontaneous recovery may aid development of novel therapies for clinical spinal cord injury.

ACUTE spinal cord injury is a common cause of disability in small animals. It may arise as a result of either external trauma, such as road traffic accidents or falls, or internal trauma, such as that associated with acute intervertebral disc extrusion. Although many affected animals do recover satisfactory function, some never regain the ability to walk.The prognosis for people who have suffered severe spinal cord injury is also poor, and provides an impetus for experimental investigations into the mechanisms of spinal cord injury and repair. This research is of particular relevance to veterinary clinicians because many experiments on acute spinal cord injury have been conducted on quadrupeds. Conversely,

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Notes