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Are oral essential fatty acids alone an effective treatment for symmetrical lupoid onychodystrophy/onychomadesis?

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Clinical scenario

A five-year-old, male neutered Lurcher dog presents to you with a history of onychoschisis on one claw progressing to onychorrhaxis and onychomadesis, which is now affecting multiple claws on all four feet and causing the dog great discomfort and lameness. A sample taken from the claw bed for cytological examination did not reveal any microorganisms, the owner consented to amputation of the third phalanx on one claw in order to collect a specimen for histological examination. The histopathology report described lichenoid and hydropic interface dermatitis. Initially the dog had partially responded to a course of oral prednisolone at 1.5 mg/kg once daily, however the owner reports that the dog was showing side effects such as urinating in the house and when the dosing was reduced to every other day, the nail condition appeared to relapse.

The question

In [dogs affected by lupoid symmetrical onychodystrophy], how does treatment with [oral essential fatty acids] compare with [other available treatment options] to improve [growth of normal nails]?

Clinical bottom line

Symmetrical lupoid onychodystrophy/onychomadesis is a complex disease with potentially multiple different causes. The most significant contributing factors identified in the literature being genetic predisposition, as seen in studies of setters and bearded collies [9,12,13], and a dietary component, with mechanical trauma exacerbating clinical signs. From the literature available recording responses to different treatment regimes, it appears that no treatment option is universally effective, however, it may be prudent to trial a diet rich in fatty acids specifically formulated for dermatoses and antibiotic therapy, in some cases, as part of the initial treatment plan, when presented with an animal suffering from this disease. Some authors report that owners perceived an improvement in the claw condition, or relapse after stopping, oral essential fatty acids and therefore they should be considered as adjunct or maintenance therapy alongside other suggested treatments such as tetracyclines and niacinamide, prednisolone or pentoxifylline. [9]

Search parameters

(exp dogs/ or dog*.mp. or canine*.mp. or canid*.mp.) and (Onychomycosis/ or onychodystrophy.mp or "claw disease".mp or onychomadesis.mp) and (tetracycline/ or exp nicotinamide/ or exp Fatty Acids/ or cyclosporins/ or cyclosporine/ or tetracycline*.mp or nicotinamide.mp or "fatty acid".mp. or "fatty acids".mp. or ciclosporin*.mp. or cyclavance.mp. or atopica.mp. or management*.mp. or treatment*.mp.)

Databases searched

CAB Abstracts 1973 to 2020 Week 02

Ovid Medline 1946-present

Search results

CAB Abstracts – 21 resources

7 resources discounted as not relevant

3 resources discounted due to texts not being available in English

4 resources not appraised as not providing case information

Remainder = 7

Medline – 14 resources

3 resources discounted as not relevant

1 resource discounted as not providing case information
7 resources discounted as duplicates from CAB Abstracts
Remainder = 3
Total papers appraised = 10

Search last performed 17 January 2020

SUMMARY OF EVIDENCE

Paper 1: Canine symmetrical lupoid onychodystrophy: a retrospective study with particular reference to management [1].

Patient group: Six dogs of five different breeds presenting with onycholysis, onychomadesis, onychalgia and onychodystrophy over a period of five years. All presented with age of onset between six months to eight years old and were confirmed as having symmetrical lupoid onychodystrophy by histopathological examination of the amputated distal phalanx.

Study type: Case series.

Outcomes: Good response entailed resolution of onycholysis, onychomadesis, claw regrowth and no further pain; with continuation of abnormal nail morphology and structure. Partial responders had continuing onychodystrophy with only occasional episodes of onycholysis, onychomadesis and onychalgia, treatment was modified where permitted by owner. Failure was defined as no improvement in the condition after starting therapy. The period of follow up varied from ten months to two and a half years.

Key results: All treatment options had varying levels of success, but none were universally effective. Two cases had received biotin and zinc supplements previously with no response.

- Three dogs received two capsules per 10 kg of essential fatty acids (552 mg linoleic acid, 68 mg gamma linolenic acid, 34 mg eicosapentaenoic acid and 22 mg docosahexaenoic acid): one good response, one partial response, one poor response.

- Four dogs treated with tetracycline and nicotinamide (500 mg of each drug administered three times daily): two good responses, one partial response, one poor response.

- One dog treated with azathioprine (2.2 mg/kg once daily) and prednisolone (1 mg/kg twice daily), good response but side effects led to complications and ultimately euthanasia.

- One dog treated with prednisolone (1 mg/kg twice daily), tapered to maintenance dose, partial response.

Study weaknesses: This case series has a small study group with no control group. The period of follow up varied from ten months to two and a half years. The measurement of response was subjective and did not consider improvement in pain or lameness.

Paper 2: Treatment of symmetrical onychomadesis and onychodystrophy in five dogs with omega-3 and omega-6 fatty acids [3].

Patient group: Five dogs with symmetrical onychomadesis and onychodystrophy between two and nine years old, treated with one to two capsules per 10 kg body weight of oral essential fatty-acids (247.2 mg linoleic acid, 30.8 mg gamma linolenic acid, 9.8 mg eicosapentaenoic acid and 6.5 mg docosahexaenoic acid per capsule).

Study type: Case series.

Outcomes: The cases were followed for up to 52 months; data was provided on the time to clinical improvement which was described in terms of claw quality and the observation of claw shedding.

Key results: In all five cases, clinical response was recorded to be good. With all cases relapsing when therapy was withdrawn. Dogs were changed from a product containing minerals and vitamins (Efa-Vet 1) to one purely containing essential fatty acids and Vitamin E (Efa-Vet Regular) with no change in clinical condition, suggesting that vitamins and minerals did not have a role in the resolution of signs.

Study weaknesses: The study group was small with no control group and the study was not randomized. Only two of the dogs were formally diagnosed with symmetrical lupoid onychodystrophy by histopathological examination. Other studies failed to reproduce the same results. A further issue was that a 'good' clinical response was not objectively defined.

Paper 3: A Retrospective Study Regarding the Treatment of Lupoid Onychodystrophy in 30 Dogs and Literature Review [6]

Patient group: Thirty dogs of various breeds, weighing between six and fifty kilograms. All dogs were diagnosed with symmetrical lupoid onychodystrophy based on history, clinical signs and histopathological changes on biopsies acquired by either onychectomy or onychobiopsy without onychectomy.

Study type: Case series

Outcomes: The response to various treatment trials, usually administered for at least eight weeks, while diet trials were followed for 6-8 weeks, was described as excellent, good, partial or poor. An excellent response was defined as complete regrowth of normal claws; a good response was defined as complete resolution of pain, onycholysis, and onychomadesis, but with continued abnormal claw morphology. Continuing onychomalacia and onychodystrophy with reduced but occasional episodes of onycholysis and onychomadesis constituted a partial response. Dogs with a poor response showed no substantial improvement.

Key results: The study showed compelling evidence of a link between diet and symmetrical lupoid onychodystrophy in one case with dietary rechallenge being performed. The author recommends initial therapy with tetracycline and niacinamide, then second line with eight weeks of pentoxifylline or essential fatty acids in cases showing an inadequate response, and immunosuppressive drugs as third line. However, the waxing and waning nature of disease making evaluation of drug efficacy difficult was acknowledged. Four different preparations of essential fatty acids were used in the study with varying amounts of omega-3 and omega-6 fatty acids, however no significant difference was noted between products.

- Treatment with tetracycline and niacinamide (doses not disclosed) yielded excellent responses in four dogs, a good response in two dogs, a partial response in two dogs, and a poor response in two dogs.
- Doxycycline and niacinamide (doses not disclosed) produced excellent responses in three dogs, a good response in two dogs, a partial response in five dogs, and a poor response in two dogs.
- Pentoxifylline led to an excellent response in two dogs, good response in two dogs and no improvement in two dogs.
- Prednisolone as sole therapy produced a good response in the one dog that received this treatment.
- Two dogs received prednisolone as well as oral essential fatty acids. Both showed good responses with no relapse in clinical signs following cessation of prednisolone or withdrawal of treatment altogether.
- One dog receiving combined therapy of prednisolone and an allergen specific immunotherapy vaccine had an excellent response.
- The one dog that received treatment with prednisolone, doxycycline and essential fatty acids had no response and was not followed up.
- One dog was treated with clofazimine, and while the initial response was excellent, six months later the dog relapsed with concurrent signs of atopy while still on treatment.
- Azathioprine with pentoxifylline produced a good response in one dog, that was then maintained on pentoxifylline.
- Sole treatment with essential fatty acid supplementation was trialled in one dog where it led to a partial response.
- Three dogs responded to a six-week course of antibiotics (two receiving amoxicillin-clavulanic acid, one cephalexin). Two of the dogs were in remission for two years without further treatment. The third dog had no clinical signs for six months, with the claw condition relapsing alongside signs of flea allergic dermatitis.
- Combined therapy with essential fatty acids alongside doxy- or tetracycline and niacinamide produced three excellent responses, with one dog maintained on tetracycline and niacinamide, one maintained on essential fatty acids and one resolving without medical intervention. Three dogs had partial responses, and a further four had poor responses. Four dogs that initially received other therapies were maintained successfully exclusively on essential fatty acids; one dog required two courses of doxycycline over two years to maintain remission.
- One dog's condition was responsive to an elimination diet and oral essential fatty acids and relapsed with diet rechallenge. In the long-term, the dog was successfully maintained on an exclusion diet, with essential fatty acids added after the dog suffered trauma to its claws.

Study weaknesses: Most of the dogs in the study group received multimodal therapy, and different products were used at differing dosing intervals making it difficult to attribute success to any one treatment. The study was neither

randomized nor controlled, and seven dogs were lost to follow up. Possible genetic cause for varying response to treatments acknowledged, however in such a varied group this was not represented.

Paper 4: A treatment study of canine symmetrical onychomadesis (symmetrical lupoid onychodystrophy) comparing fish oil and cyclosporine supplementation in addition to a diet rich in omega-3 fatty acids [11].

Patient group: Twelve Gordon setters and one English setter with age of onset of disease between the ages of three to seven years old. Dogs were recruited at the first occurrence of onychomadesis treated with either 5 mg/kg cyclosporine once daily (n=7) or 10 ml Dr Baddaky fish oil® once daily (n=7) for six months. One dog was included in both groups after developing symmetrical onychomadesis following six months of treatment with cyclosporine.

Study type: Randomized treatment trial, not blinded.

Outcomes: Number of normal claws assessed monthly for a six month treatment period. Each claw was characterised as either normal or showing signs of dystrophy. The outcome of the treatment trial was the difference between the number of normal claws for each individual at presentation and after six months of treatment.

Key results: Owners perceived that even though onychodystrophy and onychomadesis reoccurred in most dogs after stopping treatment, the reoccurrences were not associated with as severe pain and lameness as in the first instance. There was no statistical difference in number of normal claws between groups following the treatment period of six months. The author recommends omega-3 supplementation, either dietary or supplemented, as a first line treatment over cyclosporine due to high cost and apparent lack of effect.

All dogs, except one in the group receiving cyclosporine, showed an increase in the number of normal claws during the study period. There was a statistically significant improvement in the number of healthy claws after six months of treatment with a median increase of 13.5 claws for both groups.

Study weaknesses: Given that there was no significant difference in results between the two treatment groups, it could have been that feeding the dogs a diet rich in essential fatty acids (Eukanuba Veterinary Diets Dermatitis®) played as important a role in the increased number of normal nails as the prescribed therapies. Due to the waxing and waning nature of the disease, it would have been valuable to follow the dogs for a longer period of time.

Paper 5: Symmetrical lupoid onychodystrophy in a crossbred pointer dog: long-term observations [10].

Patient group: A three-year-old male crossbred pointer with a two month history of abnormal nail growth, starting on one claw and progressing to involve nails on other paws. On presentation, the dog was observed to have onychalgia, onychodystrophy, onychogryphosis and onychomadesis.

Study type: Case report.

Outcomes: Overall claw condition assessed one and three years after presentation.

Key results: After one year of mechanical treatment, the dog was no longer in pain and had no more breaking of claws. No response after one year of oral therapy with essential fatty acids; the dog was managed exclusively by trimming and filing the nails to minimize trauma. Three years after diagnosis, only mild claw abnormalities were present.

Study weaknesses: The number of nails affected is not disclosed; therefore it is difficult to objectively measure success of treatment. This was a case report following one individual on this kind of management. Unfortunately, due to the waxing and waning nature of the disease it is unclear whether this is a viable treatment option. The dose and product of essential fatty acids for weight were not disclosed, so we cannot rule out that essential fatty acids could have made a difference in this patient.

Paper 6: Symmetrical onychomadesis in Norwegian Gordon and English setters [12].

Patient group: Norwegian Gordon setters (n=18) and English setters (n=4) with symmetrical onychomadesis first showing signs between two and seven years old.

Study type: Case series with control group.

Outcomes: Measures reported included presence of normal claws, onychodystrophy claws, with/without pain, or euthanasia.

Key results: Six dogs showing clinical signs also had siblings affected, suggesting there is a genetic component of the disease. In a population of Setters, 12.6% were affected in the randomly selected control group (n=104), and 34.3% of dogs included in the study and their littermates (n=101). All of the dogs were supplemented with essential fatty acids, however very few achieved true remission. The authors report that 15 dogs developed their claw disease between

May and September during a period of more intense training, which could support the idea of mechanical stress on the nails exacerbating the disease.

Two dogs treated with prednisolone (0.5-1.5 mg/kg), fatty acid supplementation (Dr Baddaky fish oil®) and either tetracycline (500 mg TID) and niacinamide (500 mg BID) or cephalexin (25 mg/kg BID), alongside nail trimming responded well after six months, and had normal nail growth thereafter. Eleven dogs had onychodystrophy without recurrence of onychomadesis, three of these dogs were not receiving essential fatty acids as part of maintenance therapy. Six dogs continued to have intermittent onychomadesis, usually when not receiving therapy, with two owners perceiving relapse following stopping oral essential fatty acids. Three dogs were euthanized due to their disease, two while receiving treatment, one not receiving treatment.

Study weaknesses: Prior to enrolment onto this study, not all dogs received the same screening tests, with only eight dogs having haematology and blood biochemistry analysis, and eight having a thyroid profile check. Bacterial swabs were taken from only seven dogs, and three fungal cultures were performed. The dogs were assessed and treated by several different clinicians, which may have led to discrepancy in judgment of response to treatment. Multimodal treatment with different combinations and doses in some cases makes it difficult to accredit improvement to any one intervention.

Paper 7: What is your diagnosis? [2].

Patient group: An eight year old, male, neutered greyhound crossbreed with obvious claw abnormalities affecting six digits across all four feet.

Study type: Case report.

Outcomes: The case was assessed after three months of treatment for claw growth.

Key results: After three months of treatment with fatty acid supplementation at a dose of 552 mg linoleic acid, 68 mg linolenic acid, 34 mg eicosapentaenoic acid, and 22 mg docosahexaenoic acid/10kg, abnormal claws had been shed and replaced with normal claws. In this case, treatment solely with essential fatty acid supplementation appeared to lead to remission.

Study weaknesses: A follow up time of three months may not be long enough to fully assess response to essential fatty acids; improvement in such a short timescale could have been due to the waxing and waning nature of the condition.

Paper 8: Diagnosis of canine claw disease ± a prospective study of 24 dogs [7].

Patient group: Twenty-four dogs of multiple breeds aged between eighteen months and ten years old. All dogs had claw disease affecting multiple claws characterised by onychomadesis and onychomalacia with age of onset between one and ten years old.

Study type: Case series.

Outcomes: The response to a home cooked diet was assessed after 6-8 weeks in all except one dog. Response to diet trials and courses of antibiotics were reported as partial or complete resolution of clinical signs with some reference to pain, lameness, onychomadesis and onychomalacia.

Key results: Four dogs out of twenty-three being fed a home-cooked elimination diet had partial or full resolution of clinical signs, with the two dogs being rechallenged and both relapsing. One of eight dogs treated with antibiotic therapy responded fully to a six-week course (12.5 mg/kg amoxicillin and clavulanic acid BID) and remained in remission for over two years.

In two cases, adverse food reaction was confirmed as the cause of their claw disease and, although the other two dogs responding to elimination diet were not rechallenged, they were also speculatively assumed to be diet responsive. The group investigated a possible link between claw disease and vaccination and could find no relationship.

Study weaknesses: Two dogs responding partially to an elimination diet and were not rechallenged; they were therefore, speculatively assumed to be diet responsive.

Paper 9: Symmetrical Lupoid Onychodystrophy in Dogs: A Retrospective Analysis of 18 Cases (1989-1993) [8].

Patient group: Twelve dogs of varying breeds between the ages of three and eight years old received treatment with omega-3 and omega-6 supplementation (one capsule per 9.1 kg SID), oral prednisone (2.2 mg/kg SID for 10 days then tapering to alternate days) or vitamin E (400 mg BID). Each dog showed signs of onychomadesis and onychodystrophy for between one to eight months prior to claw biopsy.

Study type: Cohort study.

Outcomes: Measurement of success of treatment was defined as “good” to “excellent” in all cases. Follow up period varied within the group.

Key results: Histopathological examination of the claw specimens collected from these eighteen dogs found hydropic and lichenoid interface dermatitis. Due to the similarities with changes seen in lupus erythematosus, the condition was named symmetrical lupoid onychodystrophy.

Nine dogs that received omega-3 and omega-6 supplementation showed good to excellent response to treatment. Clinical signs improved within three to four months with maximum improvement within twelve months. Two dogs that relapsed when treatment was discontinued, both dogs achieved remission when supplementation was reintroduced.

- The three dogs being treated with oral prednisone or vitamin E supplementation showed good to excellent response to treatment.

- Two dogs that received no treatment were followed for eighteen months and two years respectively. Both dogs continued to have claw disease during this period.

Study weaknesses: The treatment group was small, particularly for dogs receiving prednisone and vitamin E, making it difficult to draw any comparison between success rates of treatment between these products and omega-3 and -6 supplementation. Measurement of success of treatment was measured subjectively, defined as “good to excellent” in all cases, which does not give a sense of whether there was complete remission of disease with normal nail growth and resolution of pain.

Paper 10: Canine symmetrical lupoid onychomadesis in bearded collies [10].

Patient group: Twenty-eight affected bearded collie dogs aged between one and nine years old and thirty-nine control dogs, also bearded collies over the age of eight years old.

Study type: Case-control study.

Outcomes Analyses were reported for the mineral composition of claw samples comparing affected and control groups. An extensive questionnaire was completed by owners to assess for environmental variables. Specific reporting of the response to administered therapies included partial or complete clinical response; response to dietary trials was given as satisfactory; quality of life outcomes were given as slight, moderate or severe impairment.

Key results: Twenty-five dogs received treatment for SLO and there was no significant association between outcome and the type of drug(s) used for treatment; improvement was recorded in 17 dogs (68%). Treatments varied in dosage, type and duration; the most used combination was fatty acids, pentoxifylline and tetracycline.

The study identified an increase in the likelihood of developing lupoid onychomadesis of 50% in dogs who started sport level exercise/training aged five months compared to those who started at fifteen months. Analysis of the mineral composition of the dogs’ nails revealed an increase in Ca, P and Na, and a decrease in Zn of affected dogs compared with the unaffected population.

Study weaknesses: The sample group of dogs that had been exercised strenuously was small (n=67) and thus the statistical analysis showing a relationship between age of starting training and likelihood of developing lupoid onychomadesis was of low power. It is notable that in this study, the control group of dogs was an older population and therefore it is unclear whether mineral components of the nails can reliably be accredited to having disease – it may be an interesting further study to compare the nails of normal dogs from different age groups in order to validate these results further.

Comments

There are limited studies available investigating symmetrical lupoid onychodystrophy/onychomadesis that directly compare essential fatty acids to other treatment options with most of the studies being case series rather than randomised control trials. This is understandable, given that often these animals present with pain and lameness, making the priority to try and achieve remission of signs as quickly as possible, which often leads to multimodal treatment being used. In the one study that compared essential fatty acids to cyclosporine under controlled conditions [10], the diet was also controlled, with dogs being solely fed a diet high in omega-3. Given that there was no statistical difference in improvement between treatment groups and evidence found in other trials [6][7][9] suggests that diet can have a role in the pathogenesis of nail disease, it is possible that it was the dietary control, rather than supplementation with essential fatty acids or cyclosporine, that led to an improvement in claw condition. However,

with at least a partial response to fatty acid supplementation recorded in six out of the seven resources where it was trialed, the authors would be inclined to assume that they might be beneficial in the treatment of symmetrical lupoid onychodystrophy/onychomadesis, in some dogs.

While treatment with tetracycline and niacinamide has been historically considered safe and effective, with some publications reporting some animals showed good to excellent responses [1][6], use of antibiotics in the absence of evidence of bacterial infection should be avoided in the first instance due to emerging antimicrobial resistance. The assessment of treatment efficacy was inconsistent between studies: one study used number of normal claws [11], while others recorded whether there was remission with or without onychodystrophy [2,8][11] and some used subjective measures e.g. excellent, good, partial, poor [1][3][6][7][8]. It is noted that in one study [1] a dog had received supplementation with biotin and zinc for its claw disease with no effect. While trials have been performed in humans and provide favourable evidence for the value of biotin in increasing nail thickness [4][5], a search of the veterinary literature provided no evidence of a therapeutic use for biotin in dogs.

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