Does turkey tail as an adjuvant therapy improve the quality of life of canine lymphoma patients?

A Knowledge Summary by

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KNOWLEDGE SUMMARY

PICO question

In canine lymphoma, does the supplement of turkey tail (*Trametes versicolor*) as an adjuvant therapy lead to a better quality of life than those that do not?

Clinical bottom line

Category of research question

Treatment

The number and type of study designs reviewed

One prospective case series was critically appraised

Strength of evidence

Very weak

Outcomes reported

The case series assessed appetite and activity level of the canine lymphoma patients. They also measured gastrointestinal toxicity and the incidence of neutropenia

Conclusion

This prospective case series is insufficient to support the use of turkey tail to enhance the quality of life of canine lymphoma patients. A controlled study is required to evaluate whether the use of turkey tail supplement is useful

How to apply this evidence in practice

The application of evidence into practice should take into account multiple factors, not limited to: individual clinical expertise, patient's circumstances and owners' values, country, location or clinic where you work, the individual case in front of you, the availability of therapies and resources.

Knowledge Summaries are a resource to help reinforce or inform decision making. They do not override the responsibility or judgement of the practitioner to do what is best for the animal in their care.

Clinical Scenario

A dog with multicentric lymphoma has been presented to your clinic. In human medicine, evidence has shown that a medicinal mushroom – turkey tail – could modulate the immune response in cancer patients and kill cancer cells in vitro (Habtemariam, 2020). Based on the current evidence in human medicine, your client wishes to know whether the mushroom-derived products, particularly turkey tail, can improve the quality of life of their dog alongside the chemotherapy or palliative care.

The evidence

One prospective case series (Holliday et al., 2009) was found relevant to the PICO. This case series studied the effect of a mushroom-derived supplement, in conjunction with chemotherapy or palliative treatment, on the quality of life of patients with various types of cancer. Regarding the relevance to the PICO, this Knowledge

Summary appraised the section of canine lymphoma in this case series only. Due to a lack of control in the case series, the strength of the evidence is weak.

Studies concerning other medicinal mushrooms without turkey tail or other cancer types were not appraised in this Knowledge Summary as they are considered irrelevant here.

Summary of the evidence

Holliday et al. (2009)	
Population:	Dogs with lymphoma staged from IIIA to VB, according to World Health Organization clinical staging system (Owen & World Health Organization, 1980). These dogs received various chemotherapy protocols based on Veterinary Cooperative Oncology Group (VCOG) or palliative treatments. Age, sex, breed and weight of these patients were not specified. Patients with hypercalcaemia were not excluded. Concurrent supplementation of immune-enhancement product was not specified as well.
Sample size:	Twenty-one dogs with lymphoma diagnosed by cytology. Three of them were diagnosed with T-cell lymphoma; 19 of them were diagnosed with B-cell lymphoma. One patient staged VB had pulmonary carcinoma concurrently. Four patients were diagnosed with hypercalcaemia concurrently.
Intervention details:	Each dog received immune-enhancement supplements (K9 Immunity™ and K9 Transfer Factor™), as an adjunct to either chemotherapy or palliative therapy. Chemotherapy lasted for 16–24 weeks, based on one or more of the following. When the patients relapsed, another protocol was implemented. For the lymphosarcoma (LSA) patients these included: • CHOP protocol: cyclophosphamide, doxorubicin (hydroxydaunorubicin), vincristine (Oncovin®) and prednisone. • Doxorubicin and dacarbazine • Vincristine and cyclophosphamide • L-asparaginase and lomustine • Vincristine and lomustine • Vincristine and chlorambucil • Single-agent protocol – e.g. chlorambucil or doxorubicin or lomustine The protocol of palliative treatment was not mentioned in the paper. The number of dogs receiving each treatment protocol was not stated in the paper. Immune-enhancement supplement – K9 Immunity™: • The active ingredients are polysaccharides derived from six species of medicinal mushrooms, namely *Agaricus brasiliensis*, *Cordyceps sinensis*, *Lentinus edodes*, *Grifola frondosa*, *Ganoderma lucidum*, and *Trametes versicolor*.

	• It was offered as an oral capsule, with each capsule containing a 500 mg mixture of the active ingredients. • The dose was 500 mg per 4.5 kg per day. Immune-enhancement supplement – K9 Transfer Factor™: • It contains antibodies (IgA, IgG and IgY), immunoproteins and proline-rich polysaccharide which aim to enhance the absorption of K9 Immunity™. • The immunoproteins were derived from bovine colostrum, bovine serum and chicken egg yolk. • Dogs > 11 kg received 3000 mg of this product (as one wafer) per day. Dogs ≤ 11 kg received ½ wafer per day. The immune-enhancement supplements were administered at home.
Study design:	Prospective case series
Outcome studied:	No recognised quality of life scoring was used, the following outcomes were measured in this year-long study instead: 1. Appetite and attitude level ○ The owners scored their dogs on a scale of 1 (no appetite or no interest in activity) to 5 (normal/better appetite or activity) daily. 2. Gastrointestinal (GI) side effect ○ The owners recorded the number of vomiting episodes and diarrhoea of their dogs daily. ○ Based on the owners' observations, dogs were classified into three categories – no signs of GI toxicity, grade I toxicity or grade II toxicity. ○ Grade I indicated that the dogs vomited or had diarrhoea for 3 consecutive days. Dogs with vomiting or diarrhoea for more than 3 consecutive days were assigned as grade II.
Main findings: (relevant to PICO question):	1. Appetite and attitude level ○ Appetite: ▪ None of them were reported as grade 1. ▪ 3/21 (14.28%) had grade 2. ▪ 4/21 (19.04%) had grade 3. ▪ 1/21 (4.76%) had grade 4. ▪ 11/21 (52.38%) had grade 5. ○ Attitude: ▪ None of them were reported as grade 1 or 2. ▪ 5/21 (23.80%) had grade 3. ▪ 5/21 (23.80%) had grade 4. ▪ 9/21 (42.85%) had grade 5. ○ Two dogs were lost to follow-up. 2. GI side effect ○ GI side effects, such as vomiting and diarrhoea, could be an indirect measurement of quality of life. They might impact the appetite and stress the patients.

	○ 16/21 (76.19%) reported no signs of GI toxicity. ○ 5/21 (23.80%) reported with grade I GI toxicity. ○ None of them developed grade II. ○ VCOG grading system was not used.
Limitations:	• No control patients in this study. • Small sample size and wide range of different regimes. • The demographic data of the dogs was not specified. • The disease-free interval was not evaluated in this study. • The data processing on 'appetite and attitude level' was unclear. • The description for scoring the 'appetite and attitude' were subjective and vague. The study failed to use a recognised quality of life score. • Study failed to use the standardised VCOG grading system for chemotherapy side effects. • A potential conflict of interest was identified. Aloha Medicinals Inc., the manufacturer of K9 Immunity™, employed three authors of this paper and provided funding to this project.

Appraisal, application and reflection

Holliday et al. (2009) published a prospective case series about the effect of a mushroom-derived supplement, K9 Immunity™, to the health-related quality of life (HRQoL) of canine patients with lymphoma. K9 Immunity™ contains the derivatives of six species of mushroom, including turkey tail (Trametes Versicolor), and it was offered with K9 Transfer Factor™ which contains a mixture of immunoproteins. In this year-long case series, the quality of life was measured by appetite and attitude level, and the adverse effect of chemotherapy namely gastrointestinal (GI) toxicity.

In canine cancer patients, the management aim is to achieve and sustain a good HRQoL. Three studies (Iliopoulou et al., 2013; Lynch et al., 2010; and Yazbek & Fantoni, 2005) have looked into a validated measurement of HRQoL in these patients. They have developed sets of questionnaires for owners to measure the HRQoL of their pets. In these questionnaires owners have been asked to score their pets in terms of their mental status, attitude, appetite, perceived pain level, mobility and hygiene. Owners' perception is useful to assess HRQoL of cancer patients as they are often the very first individuals to recognise behavioural changes when HRQoL starts to be compromised.

Holliday et al. (2009) only made an evaluation on 'activity and appetite level' with owners' perception, and GI toxicity which is the side effect of chemotherapy. In the measurement of 'appetite and attitude level', Holliday et al. (2009) failed to use a clear and validated scoring system. The paper also failed to use the standardised VCOG grading systems to assess GI toxicity. It therefore makes comparisons to other or future studies difficult. Other aspects of HRQoL, such as perceived pain level and mental status, have not been addressed by them either. Therefore, their case series did not fully and effectively assess HRQoL of the canine lymphoma patients.

GI toxicity includes vomiting and diarrhoea which may impact patients' HRQoL, as they create distress, pain and inappetence. However, Mellanby et al. (2003) reported that some owners perceived an improved HRQoL in their dogs despite the complication associated with chemotherapy. The measurement of GI toxicity may not truly reflect the HRQoL.

All dogs in the study received a mushroom-derived product and another product in conjunction with either chemotherapy or palliative treatment. There was no control group and therefore it impossible to establish the impact of mushroom-derived supplement on the adverse effects of chemotherapy and HRQoL

Unfortunately, the demographic data, such as age, sex and breed, was not specified. Together with the small sample size (n=21), it is questionable whether this case series represents the wider canine lymphoma population.

A potential conflict of interest is identified in this study. Three of the authors of this paper were employed by Aloha Medicinals Inc., which is the pharmaceutical company manufacturing the immune-enhancement supplement used. In addition, the study was funded by this company. Given a lack of control in this study, there is a risk of bias in data presentation which the readers should be cautious about.

The Holliday et al. (2009) case series should be considered a preliminary study that may show the potential of mushroom-derived supplements in improving the HRQoL of canine lymphoma patients. However, the overall strength of evidence is very weak due to the absence of a control population, incomplete assessment of patients HRQoL, failure to use the VCOG grading system for all side effects, questionable representativeness to the canine lymphoma population, and the limitations in the study design. This prospective case series is insufficient to support the use of turkey tail-derived products to enhance the health-related quality of life of canine lymphoma patients receiving conventional therapies.

Methodology Section

Search Strategy	
Databases searched and dates covered:	CAB Abstracts 1973 – 2021 Week 14 PubMed NCBI 1960 – 2021 Apr
Search terms:	CAB Abstracts: 1. dog or dogs or canine* or bitch* or exp dogs/ or exp bitches/ or exp canis/ 2. cancer* or tumour* or tumor* or malignan* or neoplas* or lymphoma* or lymphosarcoma* or exp cancer/ or exp neoplasms/ 3. (mushroom* or fungus or fungi or 'turkey tail' or yunzhi or yun-zhi or 'yun zhi' or ((Trametes or Coriolus or Polyporus) and versicolor)) 4. 1 and 2 and 3 PubMed: (dog[Title/Abstract] OR dogs[Title/Abstract] OR canine[Title/Abstract] OR bitch[Title/Abstract]) AND (cancer[Title/Abstract] OR tumour[Title/Abstract] OR tumor[Title/Abstract] OR neoplasm[Title/Abstract] OR lymphoma[Title/Abstract] OR lymphosarcoma[Title/Abstract]) AND (mushroom OR fungus OR fungi OR 'turkey tail' OR yunzhi OR yun-zhi OR 'yun zhi' OR ((Trametes OR Coriolus OR Polyporus) AND versicolor)) AND veterinary [sb]
Dates searches performed:	12 Apr 2021

Exclusion / Inclusion Criteria	

Exclusion:	• Irrelevant to the PICO:
	  ○ Species other than canine
	  ○ Turkey tail was not included in the adjuvant supplement
	  ○ Studies which did not involve lymphoma
	• Reviews, book chapters or conference proceedings
	• Articles not written in English

Inclusion:	Any published paper relevant to the PICO and available in English.

Search Outcome

Database	Number of results	Excluded – Irrelevant	Excluded – Book chapters/reviews/conference proceedings	Excluded – Non-English articles	Excluded – Duplicates	Total relevant papers
CAB Abstracts	299	296	2	0	0	1
PubMed	420	420	0	0	0	0
Total relevant papers when duplicates removed						**1**

CONFLICT OF INTEREST

The author declares no conflict of interest.

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