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Mistletoe therapy, a boon to cancer treatment

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INTRODUCTION

Widely increasing access to internet, databases and electronic communications the incidence of using alternative therapies and complementary medicine as a treatment of choice in chronic and challenging or incurable diseases is ever increasing. Surprisingly the application of CAM-therapies in all the areas of healthcare system is not well disseminated to public domain.² Major dilemma is about effectiveness of remedies and therapies to judge supplied information and its rationale in clinical practice.³

Historical intentions to use the mistletoe in Europe was restricted to swellings or tumors, epilepsy, diseases of spleen and liver, labour-pains, 'weakness of the heart' and oedema, eczema, ulcers of the feet, burns, and granulating wounds.¹⁹ Dr Rudolf Steiner (1861-1925) has introduced mistletoe extracts for cancer treatment first time ever in history of medicine.²⁴ He recommended a drug extract produced in a complicated manufacturing process combining sap from mistletoe harvested in the winter and summer¹⁴ and as described in the various Homoeopathic Pharmacopeias. As on his documentations,¹ several doctors have treated their cancer patients with these extracts within the last century. Moreover, pharmacological studies on the suggested anti-tumor effects of were completely evident.

Vester and Nienhaus isolated carcinostatic protein fractions which were recognized later as the cytotoxic viscotoxins and mistletoe lectins in 1960.²⁷ Induction of apoptosis, stimulation of immune competent cells and protection of mononuclear cell's DNA are some of the newly proven and confirmed effect of mistletoe as shown by recent research and experimentations.³⁴ Immunomodulatory effects are totally credited to the alkaloid content of mistletoe such as viscotoxins, lectins and several other components.²²

In vivo and *in vitro* study also shown the anti tumor metastatic activity of the cytotoxic mistletoe lectins results in destruction of tumor.⁵ increased survival of animals might be an effective evidence for pharmacological mechanism.¹¹ This

can also be proven with the clinical evidences such as successful treatment of metastatic malignant melanoma.⁶

Conventional medicine Versus Mistletoe therapy in treatment of cancer:

Commonly available brand of an extract of *Viscum album*, European species of mistletoe derived from various sources, is named as Helixor, Iscar, Lektinol etc. In 20th century it became slowly popular for its enigmatic use in cancer therapy. Rudolf Steiner hypothesized that human body is subject to various forces, some of which result in cell growth and multiplication ("lower organizing forces")²⁴ and some of which control and organize cell growth to form tissues and organs ("higher organizing forces"). Steiner believed that the balance between these forces determined an individual's susceptibility to cancer, with a serious imbalance promoting the development of cancer. Also considered mistletoe to have a several properties that gave it could resist natural forces³⁸, and he therefore proposed that higher organizing forces which were deficient in cancer patients; the preparations would stimulate the "higher organizing forces in same patients".⁹

Not only improvement in the survival of the patient but also reversion of cancer cells to most differentiated form and thereby reducing the tumor.²³ It has shown its marvelous results in many patients of cancer of cervix, breast, stomach, ovary, colon, lungs etc. General well being and symptomatic relief couldn't be only theme of this therapy.⁴² Administration of the Mistletoe Therapy is through parenteral mode with the regimen varying from several weeks to months in ascending dosage until a desired dosage has been reached; depending upon the size of tumor and general condition of the patient.³¹

Looking in to conventional anticancer treatment cytotoxic and hazardous drugs is used as a modality. Besides number of clinical trials in oncology the evidence remained is although efficacious but not a safe.²⁶ Many human ethical issues aroused from hundreds of eyes watching over this nihilistic and orthodox school who labeled phenomena as chemotherapy.^{7,14, 23} Many drugs on alkaloid chemistry were come in market ranging from cisplatin to podophyllotoxin as well as carboplatin, vincristine and many others. These all drugs made a terrific vigilance in society which indeed couldn't satisfy the need for novel drug discovery to treat and to cure.¹²

Concomitant introduction to oncosurgery and radiation therapy didn't disclose the chapter of justifiable approach and management in cancer population. Healthcare and support group never suffice to the achieving of terminus besides counseling.^{3, 4, 15}

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Mistletoe Therapy is a complementary medicine as well as alternative.^{17, 39} Convincing efforts for eradication of this monster will not be a job of single as well as monotherapy which in fact explains the innovative and through experimentations of phytochemical substances.

Risk and benefits involving the therapeutic application of Mistletoe Therapy:

Intention to treat is the prime and foremost responsibility of physician in the treatment of his concerned patient during clinical trial or his natural illness especially in cancer patient. Nevertheless evidence based medicine provided a key option serving in management of cancer patients.

Therapeutic index and toxicological assay of the mistletoe didn't reveal any serious effects from literature review. Increase in body temperature, chills and headaches with local inflammation at injection site were some of factor of concerns. Some constituents may cause seizures, bradycardia or even death only after unsupervised ingestion of a plant.

Adverse interactions with cytotoxic chemotherapy also seen in some studies reporting that it stimulates DTH (delayed hypersensitivity) reactions in conjunction with commonly used medications known to cause skin reactions, such as antibiotics, antiretroviral and antihypertensives. Allergic reactions to this natural product are also on a list.

Multiple scientific reports suggest that Mistletoe Therapy augments the immune response. Mistletoe Therapy has been shown to increase natural-killer cell function and antibody dependent cell-mediated cytotoxicity, enhance cytotoxicity of granulocytes and macrophages, and heighten DTH response. Mistletoe Therapy has also been shown to stimulate T lymphocyte migration in vitro. In one of these series, *Viscum album* treatment was associated with an improved quality of life^{44,45}. Chronic toxicity reported was about lectins which were cytotoxic by inhibiting protein synthesis at the ribosomal level.

Review of Meta analysis of effect of mistletoe preparations on cancer patients:

Efficacy of Mistletoe Therapy is still discussed controversially because the question certainly arises, whether the reported associations in the non-randomized matched-pairs studies between survival and therapy with the mistletoe preparation were effects of unknown origin or causally related to this therapy³². The causal character of an association include strong association, temporal sequence, consistency of results with results of studies with different design and different populations, dose response relationship, biological plausibility of clinical effects. Although biases and

confounding factors couldn't be overruled, the only credit never goes to the mistletoe preparations for survival in cancer patients.³³

Tolerability and safety issue is not always well supported with the clinical records and statements. Number of adverse events favoring the index is not enough to reach a prominent conclusion²⁹; similarly survival rate in randomized as well as nonrandomized trials does not clarify the clinical decision for universal use of the remedy.³⁵

Significance of methodological overviews in the determination of efficacy of mistletoe never fits in traditional trial design¹¹ perhaps it gets breakthrough in the case reports and its wide acceptance in day to day clinical oncological practices.

DISCUSSION

Consistency of results across the survival analysis of increasing quality of life in cancer population is still provided by some evidence of clinically relevant prolonging effect of Mistletoe Therapy as shown by many randomized as well as clinical trials. The baseline values and results are also not very significant yet stand in between stronger validity and generalizability.^{5, 6, 7, 8}

The potent anticancer activity of *Viscum album* preparation (Mistletoe Therapy) was previously known; moreover, its usefulness in inhibiting the recurrence of tumor has been documented.^{1, 2, 45} Similarly Mistletoe Therapy to inhibit chemically induced carcinogenesis has also been reported. It could be postulated from these observations that the active component in Mistletoe Therapy may retard the growth of transformed cells by inhibiting some of the cellular events that lead to cell proliferation. The mechanism of action of the extract may be related to its specific reversal of the oncogene activation cascade.

Pooled analysis of clinical studies suggests that adjuvant treatment of cancer patients with Mistletoe Therapy is associated with a reduction in mortality rates.^{12, 41} Future studies evaluating the effects of Mistletoe Therapy should continue to address this question, with a particular focus on a transparent design and description of endpoints in order to provide greater insight into a treatment often being depreciated as ineffective.

CONCLUSION

Extracts of mistletoe have been used for medicinal purposes for several decades and are known to contain alkaloids with cytotoxic effects in vitro and in vivo. Earlier knowledge about mistletoe proceeded in successful

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completion of clinical utility in practitioner's faculty and an insight into a healthcare domain.

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