

EDITORIAL

Mistletoe Treatment for Cancer—Promising or Passé?

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Editorial to accompany the article “Quality of life of patients with advanced pancreatic cancer during treatment with mistletoe—a randomized controlled trial,” by Wilfried Tröger, Danijel Galun, Marcus Reif et al. in this issue of *Deutsches Ärzteblatt International*

The recent advances in oncology are plainly evident: more than half of all persons with cancer in Germany now survive their illness and are considered cured (1). Many types of cancer can be kept under control for a long period and converted into a disease with a chronic course and an acceptable quality of life (2). Unfortunately, some cancers still regularly lead to the death of the patient within a short time. Superficially considered, these diseases may seem to be a matter of fate that cannot be influenced by any type of treatment. In fact, however, physicians have many options at hand when treating patients nearing their life’s end, and there are many medical decisions to be taken. Pancreatic carcinoma is nearly always fatal; yet, even for this disease, further treatments have recently become available. New therapeutic approaches prolong survival and improve the manifestations of the disease and the patients’ overall quality of life (3).

The role of mistletoe in cancer treatment

In this issue of *Deutsches Ärzteblatt International*, the results of a prospective, randomized drug trial are presented. It measures the effect of subcutaneously injected extract of mistletoe grown on oak trees on the quality of life of patients carrying a clinical diagnosis of pancreatic carcinoma (4). The initiators of the trial are to be commended for their attempt to provide evidence for the role of mistletoe treatment in oncology with objective data.

It is a good thing that this trial was published. This trial is a contribution to the evidence base and thus worthy of attention, even though it was indirectly financed by the drug manufacturer, as were the authors themselves. 220 Serbian patients were randomly assigned either to a group that was given subcutaneous injections of an extract of mistletoe or to an untreated control group. Both groups received symptomatic treatment of pain, nausea, vomiting, and digestive disturbances. The patients treated with mistletoe were found to have a better quality of life; nonetheless, this trial leaves some important questions open.

The validity and generalizability of the results would have been enhanced if the trial had been carried out in multiple centers, as other trials were, rather than in a single center. The authors explain why they could not perform a blinded trial, but the

lack of blinding still makes it impossible to tell with any certainty whether the effect that was found was not, in fact, a placebo effect. It would also have been better if the diagnosis of pancreatic cancer had been histologically confirmed in all 220 patients, not just in 43 of them; in most cases, the diagnosis of incurable pancreatic cancer was based on the constellation of clinical findings. In contrast to the usual procedure, it was the oncological consultation service of the department of surgery that decided whether an established type of antitumor therapy should be attempted or whether the patient should be considered as a candidate for the mistletoe trial instead. It is to be hoped that all of these factors did not distort the results of the study. The study methods are discussed critically and more in detail elsewhere (5).

Will the results on mistletoe treatment in pancreatic cancer that are presented here affect my future conversations with patients suffering from advanced cancer and my treatment recommendations for them? I think not. Aside from reservations concerning the methods of the trial, it needs to be pointed out that, in the meantime, medical science has progressed. New and more effective treatments have been introduced, including drugs, multimodal therapeutic approaches, and optimized methods of palliative and supportive care (6). A new understanding of multi-professional patient care has emerged, as have new structures for palliative treatment. Mistletoe has been used to treat cancer patients for a century, and this era, which has been mostly one of therapeutic impotence, is now ending. The context of the present trial among the other mistletoe trials performed to date in various countries also warns us to interpret it cautiously: a Cochrane review came to the conclusion that the overall quality of mistletoe extract trials leaves much to be desired (7). The authors of the present trial conclude that some of their findings indicate an improved quality of life, but they rate evidence for prolonged survival as weak.

The popularity of botanical extracts

Botanical extracts are popular in Germany. It has been reported that, in 2003, the German statutory health-insurance carriers paid the equivalent of 283 million U.S. dollars for such preparations (8); 465,000 prescriptions for mistletoe extracts were issued, making this particular type of extract an

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important part of the total (9). Outside Germany, this state of affairs often meets with incomprehension (8, 9). We should ask ourselves whether the limited resources of our health-care system ought not to be invested elsewhere.

The use of mistletoe extracts began in 1916 and can be traced back to Rudolf Steiner (1861–1925), the founder of anthroposophy. Mistletoe extracts contain a number of biologically active compounds, including lectins, viscotoxins, flavonoids, and membrane lipids. Lectins can induce apoptosis and stimulate components of the immune system (9). In Rudolf Steiner’s time, controversy surrounded both his person and his ideas (10); still today, a polarized debate about anthroposophic medicine runs through our society (11). In the 1920s, the *New England Journal of Medicine* published multiple articles on the treatment of hypertension with mistletoe extracts (12), but, as the pathophysiology of hypertension became clearer and effective treatments for it were developed, mistletoe disappeared from cardiovascular medicine. Something similar may well happen in the domain of oncology.

Treating patients at the end of their lives

We have learned that treatment recommendations at the end of life need to be considered carefully. Nihilism is out of place. The effect of antitumor treatments on the duration of survival, the burden of symptoms, and the quality of life have sometimes turned out to be stronger than expected (13, 14). The personal attention of medical caregivers, and non-pharmacological treatment by a multiprofessional team, are also effective. The early integration of palliative care positively affects both the duration of survival and on the quality of life (6). On the other hand, too aggressive treatment at the end of life can have a negative effect on the course of the illness (15). It remains one of the basic responsibilities of the physician to accompany and advise patients whose lives are drawing to a close in whatever way is best for each individual patient.

Conflict of interest statement

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