TRANSLATION

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M. Hecker

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Efficacy and tolerance of ivy extract in patients suffering from respiratory tract diseases

M. Hecker

In 2 post-marketing observation trials the efficacy and tolerance of a special dried ivy leaf extract (Prospan®) in various forms of administration (cough syrup and effervescent cough tablets) were determined in a total of 248 patients who were suffering from inflammatory diseases of the respiratory tract. Therapy proved to be effective and very well tolerated, whereby the results of controlled clinical studies with a larger range of administration were confirmed.

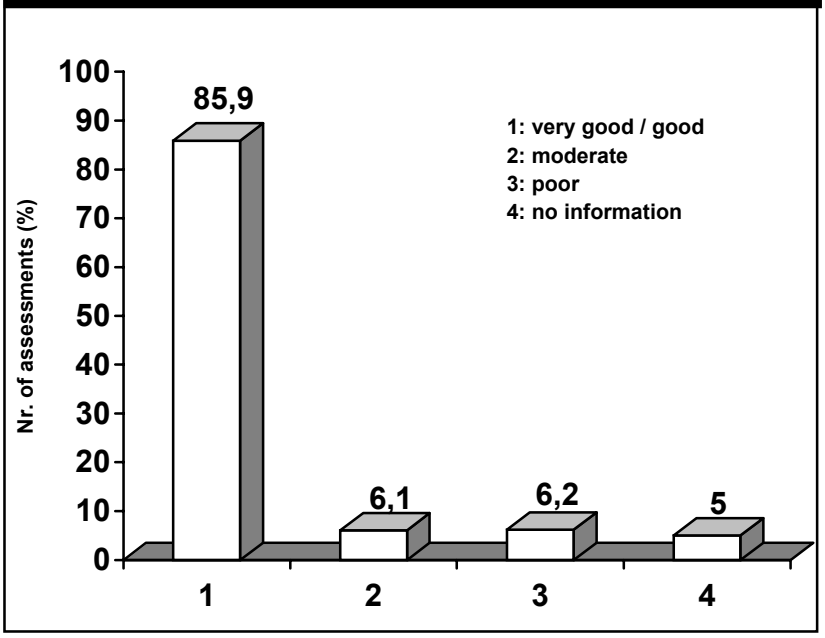
The dried ivy leaf extract, manufactured according to a special procedure, used for the studies is an expectorant, which has been on the market for more than 25 years. This expectorant is administered to adults and children of every age with the indication "acute catarrh of the respiratory tract accompanied by coughing, symptomatic treatment of chronic bronchial diseases". The product has an expectorant and anti-obstructive effect due to its secretolytic and bronchspasmolytic properties. The efficacy and very good tolerance of the various forms of administration has been proved through the results of clinical studies (1-5). In a double-blind, placebo-controlled trial, the special extract proved, with regard to an improvement in pulmonary function in patients suffering from bronchial asthma, to be clinically clearly and statistically significantly better than placebo (5). Furthermore, it was proved that aqueous preparations for oral administration have to be dosed approximately 2.5 higher than ethanolic forms of administration (2,4,6).

The recommended dosages for the corresponding prepa-

rations were therefore adjusted.

Far-reaching findings as to the efficacy and tolerance of these dosages from daily medical practice should be documented in the present post-marketing observation trials.

Fig. 1: Overall assessment of efficacy by physician



Methods

The open, multicentrically designed post-marketing observation trials, without control groups, were carried out according to the requirements of the German Drug Law, the declaration of Helsinki/ Tokyo and the principles of good clinical practice on medicinal products.

Efficacy was assessed by the doctor and noted on a 4-level scale from "symptom-free" to "worsened", with reference to symptoms and signs. Individual dosages as well as the duration of treatment were recorded as additional parameters. The assessment of tolerance resulted from the occurrence of adverse events and from a general assessment made by the individual doctor.

Patients

248 patients at an age of 0 to 79 years were included in the documentation.

Inclusion criteria

- Patients of both sexes suffering from inflammatory and /or obstructive diseases of the respiratory tract.
- Effervescent cough tablets: age ≥ 4 years
- Cough syrup: age 0-9 years

Exclusion criteria

- Treatment with another expectorant or antitussive
- Known fructose intolerance (due to the content of sorbitol)
- Intolerance to one of the components
- Severe diseases of the respiratory tract (bronchial asthma, mucoviscidosis, quinsy angina, bronchopneumonia).

Medication

The dosage and duration of treatment were based on the recommendations stated in the patient information leaflet and were adapted according to each individual clinical

picture and course of disease.

Evaluation

Qualitative characteristics were described in detail by means of a descriptive process; quantitative characteristics by means of descriptive parameters. The evaluation of tolerance took place with the Intention-to-treat Population (ITT), the analysis of efficacy was carried out with the Per-Protocol-Treatment Population (PPT). Missing values remained as such.

Results

Patients

A total of 248 patients (138 female, 110 male) were admitted to the study; 176 (71%) thereof were younger than 15 years. 120 patients were treated with cough syrup and 128 with effervescent cough tablets. 13 patients were excluded from the analysis of efficacy due to violation of the admission and exclusion criteria.

The most frequently cited indications were "bronchitis" (45%) and "respiratory tract infection" (29%). All patients apart from one suffered from cough, more than half (63%) expectorated, in 16% and 23% of the patients, shortness of breath and respiratory pain were diagnosed respectively (multiple entries were possible).

Duration of therapy

The mean duration of therapy lay at 7.3 (± 2.4) days in the case of cough syrup and at 8.2 (± 2.5) days for effervescent cough tablets within the range recommended by the manufacturer.

Dosage

76% of the patients received doses according to the manufacturer's recommendations. 12% of the patients were given less and 12% more medication than was recommended.

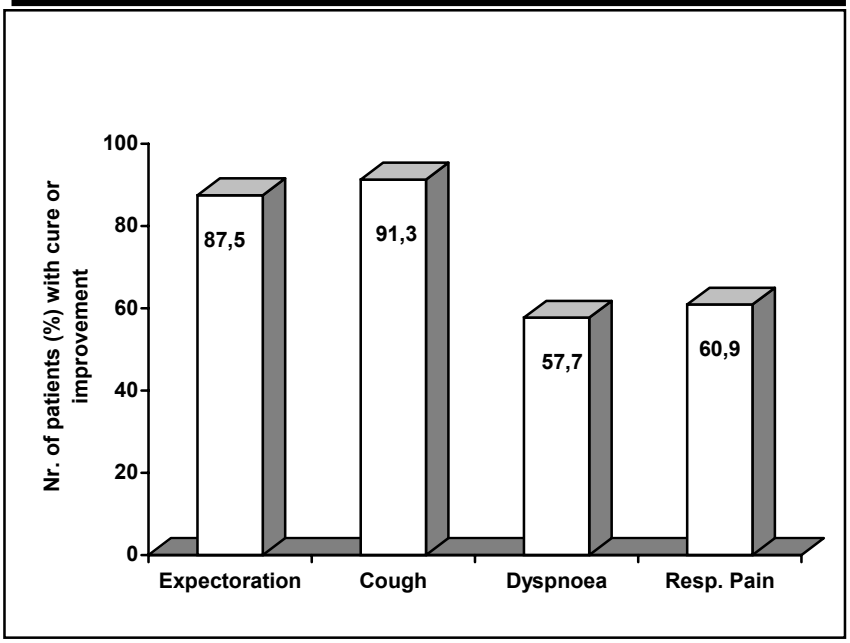
Efficacy

Efficacy was recorded on the basis of both changes in the individual symptoms (coughing, expectoration, shortness of breath, respiratory pain) and on a general assessment made by the treating doctor. With respect to the general assessment, efficacy was documented as very good to good in 86% of the patients (fig. 1). In the case of changes in individual symptoms, cough and expectoration was either cured or had improved in approximately 90% of all patients; the curing or improvement of shortness of breath and respiratory pain was obtained in approximately 60% of all (fig. 2).

Tolerance

Tolerance of therapy was judged as very good to good in 98% of all patients (fig. 3). An adverse event (allergic exanthema) was documented in only one patient, the connection of which to the medication was however not specified.

Fig. 2: Curing or improvement of symptoms



Discussion

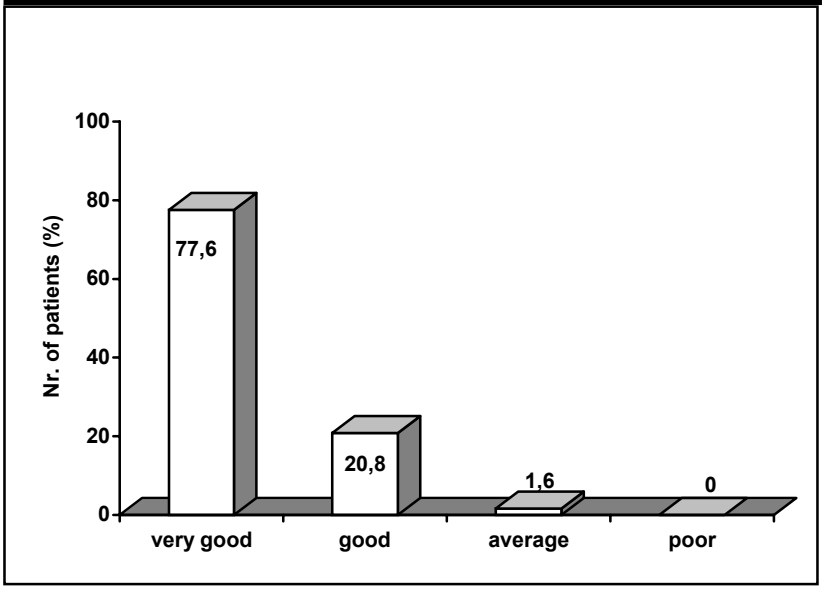
The hereby examined special dried ivy leaf extract has been used for more than 25 years in varying forms of administration. A positive monograph on the substance was published in 1988 by the Federal Public Health Department (BGA), in which a daily dosage of 300 mg of drug was considered sufficient. This monograph was based on results using an ethanolic preparation (47% ethyl alcohol) of the active ingredient. As ethanol is commonly known as being a resorption mediator, the issue is to be settled, as to whether higher doses of ethanol-free administration forms of the active ingredient are eventually necessary, in order to be of therapeutic equivalence, when compared to an oral, ethanolic preparation. In a controlled clinical trial (2) as well as in a post-marketing observation study (6), it was demonstrated, that an approximately 2.5 times higher dose of the aqueous administration form was needed for oral application, so as to be able to achieve a comparable effect to the ethanolic administration form. The manufacturer's dosage recommendations or Prospan® take these findings into account.

During the present post-marketing observation studies, the medication was given to 76% of all patients according to the manufacturer's recommendations. The results prove the efficacy and tolerance of these dosages in patients suffering from inflammatory diseases of the respiratory tract. The documentation on efficacy is of significance especially with respect to the symptoms "cough" and "expectoration", as practically all patients were suffering from cough and more than 60% from expectoration (whereas shortness of breath and respiratory pain was diagnosed in only 16% and 23% of patients respectively) before treatment.

Tolerance of therapy was very good. An adverse event (allergic exanthema) was documented in

only one patient, the connection of which to the medication was however not specified. Furthermore, the patient was being simultaneously treated with the active ingredient paracetamol, for which there have been reports of rare cases of allergic skin reactions.

Fig. 3: Tolerance of therapy



Conclusion:

These post-marketing observation studies demonstrate that the different dosages of the various administration forms of dried ivy leaf extract established in clinical trials are also valid in wide medical practice, with regard to the efficacy and excellent tolerance of Prospan®.

Correspondence to:
Dr. Martina Hecker,
Katharina-Schackey-Str. 5a, D-61169 Friedberg

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