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Studies on the therapeutic efficacy of Echinaforce®

Phytotherapy for the adjunctive treatment of recurrent infections of the respiratory tract

The aim of the present study was to investigate the therapeutic efficacy of Echinaforce administered as «adjunctive treatment of recurrent infections of the respiratory tract» as exemplified by upper respiratory infection (influenza-like infections, common cold), and to investigate the tolerability of Echinaforce. Echinaforce is an mixed alcoholic extract made from the stems and leaves, together with the root, of Echinacea purpurea. The study was designed as a multicentric, uncontrolled open trial, and was carried out between September 1989 and April 1990. Participants in this trial were four general practitioners working in three practices, who recruited a total of 77 patients with upper respiratory infection, and treated them with Echinaforce. The dosage of Echinaforce applied was 3 × 30 drops a day, administered orally for a period of 14 days. The entire observation period was, on average, 28 days.

The proof of efficacy provided by the present study was based on the amelioration or healing of the upper respiratory infection during the period of observation, and on the subjective assessment of the overall efficacy and tolerability by both patients and physicians.

For the establishment of the diagnosis and assessment of the severity of the illness, a summed score of a range of clinical symptoms was established and defined as the symptoms index. The average symptoms index underwent an appreciable decrease during the course of the observation period, reflecting an improvement in the symptoms of the infection. Accordingly, the therapeutic efficacy was assessed by both patients and care-providing physicians to be clinically relevant. Tolerability was rated good by 76 patients and the care-providing physicians. Only a single patient abandoned treatment on the fourth day on account of nausea, restlessness and aggravation of the overall symptomatology. This patient was taken into account only for the assessment of tolerability. The remaining patients took Echinaforce in accordance with the protocol, without experiencing any untoward effects, right up to the end of the trial. The present clinical study shows both that the administration of Echinaforce brings about an appreciable improvement in the symptomatology of upper respiratory infection, and that the preparation is extremely well tolerated.

Herbal immunostimulants have been successfully employed in folk medicine for hundreds of years under the names alterants (alteratives, alterative medicines), influenza remedies or irritative (stimulative) substances. Among these phytotherapeutic restoratives used to stimulate the body's own defences, extracts of echinacea have a prominent role to play (1, 2). The plant was originally employed as a remedial by the North-American Indians. Later, echinacea was discovered by the white settlers, who used it for a long time as a remedy for infectious diseases. Finally, the plant was brought to Europe at the beginning of the present century and began its triumphal victory march here, too. Whether used by the native peoples of America or by modern Europeans, the range of indications for echinacea have undergone no major changes. Extracts of echinacea are employed in particular for the treatment of chronic inflammatory diseases of the respiratory and urinary tracts, and for the prevention of infection (3, 4). The well-tested

traditional application of echinacea has been confirmed by modern pharmacological (5, 6) and clinical (7, 8) investigations that have demonstrated the immunostimulatory effect of extracts of the plant. Of decisive importance in this connection was the development of numerous test systems for assessing immunologically active substances which, for a number of years, now, have made it possible to provide scientific confirmation of traditional empirical knowledge (9, 10, 11, 12).

Echinaforce is an mixed alcoholic extract made from the leaves and stems, together with the roots, of Echinacea purpurea. Various investigations have shown that extracts of echinacea do not exercise any direct action on the pathogens responsible for the disease, but develop their positive effect indirectly via stimulation of the unspecific immune system. This stimulation of the unspecific immune system by medicinal substances is known as immunostimulation. The unspecific immune system comprises a cellular (granulocytes, macrophages) and a hormonal (lysosome, interferons) component, which phagocytose or destroy the invading pathogens. To date, little is known about the mechanisms behind the herbal stimulation of the immune defence system.

Since this immune response is a highly complex occurrence, the therapeutic efficacy of immunostimulants depends on numerous factors, for example the immune status of the patients, the timing of their administration, the dosage given, and the mode of administration. The results obtained to date with echinacea preparations in pharmacological and clinical studies on efficacy are promising.

In summary, they show that extracts of echinacea can be used – in accordance with the present state of our knowledge with good reason and chances of success – in the prophylaxis of recurrent infection of the upper respiratory tract and the efferent urinary tract, as also as adjuvant treatment of bacterial infections and the treatment of chronic inflammatory diseases in general.

Aim and conduct of the study

The aim of the study was to establish the efficacy and tolerability of Echinaforce used as adjunctive treatment of upper respiratory infection, on the basis of the assessments made by the patients and care-providing physicians on the one hand, and undesirable side effects on the other.

Study design

The study was designed as a multicentric, open phase IV trial, and was conducted in Austria (13).

A total of 77 patients took part in the trial. Prior to, during and following treatment with Echinaforce, each patient was seen by the care-providing physician on four occasions, namely, on days 0, 3, 8 and 28.

Patient selection

The participants in the study were recruited from the patients of four general practitioners working in three practices in Austria. All the patients were informed about the purpose of the study before being included, and they all gave their written consent to participate.

Inclusion criteria

- Upper respiratory infection
- Age between 30 and 71 years
- Maximum duration of the illness prior to the start of treatment, 3 days.

Exclusion criteria

- Simultaneous use of antibiotics and/or antihistaminics
- Use of immunostimulants within the four weeks prior to the start of the trial
- Severe concomitant diseases

Recording of diagnosis and symptoms

Prior to the start of the study, a symptoms index was established for each patient to characterize the severity of his/her disease **(Table 1)**. On the one hand, this permitted the establishment of the diagnosis of «influenza», while on the other, the severity of the disease was categorizable by means of a single number. The higher the symptoms index, the more severe was the dis-

URI Symptoms	Score none - mild - moderate - severe
Fever	0 - 1 - 2 - 3
Joint pain	0 - 1 - 2 - 3
Circulatory insufficiency	0 - 1 - 2 - 3
Sweating	0 - 1 - 2 - 3
Dizziness	0 - 1 - 2 - 3
Headache	0 - 1 - 2 - 3
Cough	0 - 1 - 2 - 3
Head cold	0 - 1 - 2 - 3
Sore throat	0 - 1 - 2 - 3
Difficulty in swallowing	0 - 1 - 2 - 3
Earache	0 - 1 - 2 - 3
Drowsiness	0 = no 1 = yes
Nausea	0 = no 1 = yes
Sum of the individual symptoms = symptoms index (maximum 35)	

Table 1: Assessment scale of the symptoms of upper respiratory infection (URI)

Score	Assessment	Clinical significance
1	very good	clinically relevant, i.e. well tolerated
2	good	
3	satisfactory	
4	poor	clinically not relevant, i.e. poorly tolerated
5	very little	
6	none	

Table 2: Rank scale system for the subjective assessment of overall efficacy and tolerability

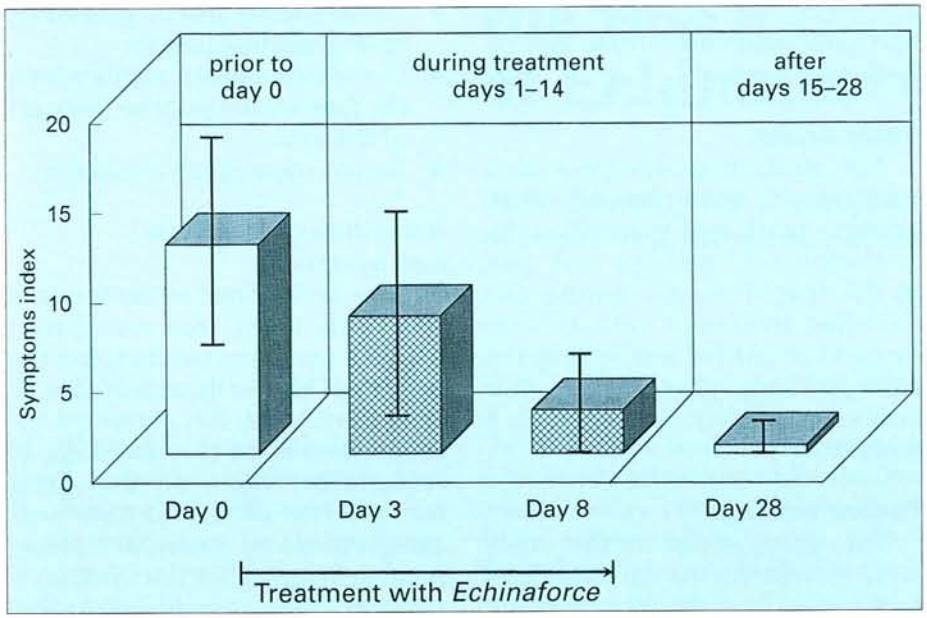

Figure 1: Decrease in the symptoms index during the period of observation. Symptoms index + standard deviation of Echinaforce, documented prior to the start of treatment (day 0), during treatment (days 3 and 8), and after treatment (day 28) in 76 patients with upper respiratory infection.

ease. For the establishment of the diagnosis of an upper respiratory infection, an index of at least 6 was required. For maximum severity of the illness, the index would have a value of 35.

Test preparation, duration of treatment and dosage

The participating physicians were supplied with the test medication in dropper bottles. The fresh-plant test preparation, Echinaforce, comprised 95.0 g Echinacea purpurea tincture obtained from the fresh leaves and stems, and 5.0 g Echinacea purpurea tincture obtained from freshly gathered roots. The alcohol content of the tincture was 57%. Dosage instructions were as follows: 30 drops 3 times a day in a little water and taken in several sips.

This daily dose of 90 drops was within the dosage range of 20–25 drops 3–5 times a day (60–125 drops daily) that is recommended for the Swiss-registered product.

Concomitant medication

The simultaneous use by the patient of antibiotics and/or antihistaminics was expressly forbidden. Other medications were allowed, but had to be scrupulously noted.

Proof of efficacy and tolerability

The proof of efficacy was to be established on the basis of an evaluation of the following parameters:

- Elimination or amelioration of the symptoms as documented by a decrease in the symptoms index during the course of the observation period of four weeks.
- A separate subjective overall assessment by the patients themselves and the care-providing physicians using a rank scale system **(Table 2)**.

Tolerability was tested on the basis of the following parameters:

- Recording of side effects as noted by the care-providing physician
- Separate establishment of the subjective assessment of overall tolerability by patients and care-providing physicians using a rank scale system **(Table 2)**.

Statistical analysis

For the evaluation of the demographic data and the information (from patients and physicians) on efficacy and tolerability, average and percentage calculations were employed.

Results

Patient group

Among 77 patients, 76 were evaluated for the establishment of efficacy, and 77 for the assessment of tolerability.

The age of the patients ranged between 30 and 71 years (average age 47 years). None of the participants used any forbidden concomitant medication.

Proof of efficacy

Change in symptoms

On the days on which the doctor examined the patient prior to (day 0), during (days 3 and 8) and after (day 28) treatment with the test preparation, average symptoms indexes (including standard deviation) were established on the basis of the 13 symptom scores. An appreciable, constant decrease in the average symptoms index from 11.67 at the start of therapy (day 0) to

URI Symptoms	Change in symptoms index % initial value	Clinical effect
Fever	88%	improved
Joint pain	79%	improved
Circulatory insufficiency	65%	improved
Sweating	74%	improved
Dizziness	76%	improved
Headache	75%	improved
Cough	71%	improved
Head cold	79%	improved
Sore throat	88%	improved
Difficulty in swallowing	88%	improved
Earache	87%	improved
Drowsiness	0%	unchanged
Nausea	0%	unchanged

Table 3: Improvement in the individual symptoms under treatment. Percentage change in the average symptoms index of the individual symptoms prior to (100 %) and after eight days of treatment with Echinaforce.

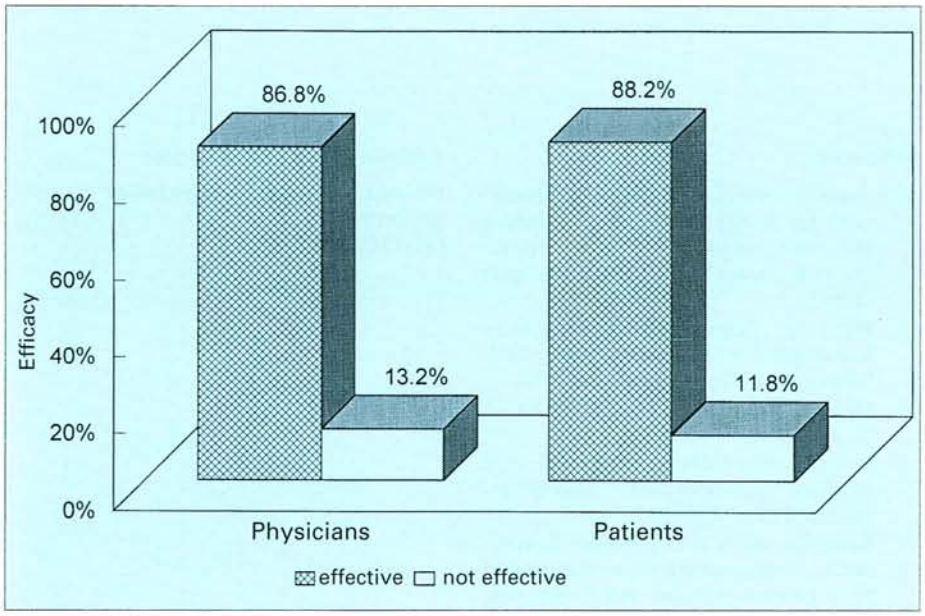

Figure 2: Subjective overall efficacy of Echinaforce in the view of the patients and care-providing physicians. The clinically relevant efficacy (very good, good, satisfactory) was represented as effective; clinically non-relevant efficacy (poor, very little, none) as not effective. A total of 76 patients were assessed.

0.45 at the end of the period of observation (day 28) was noted.

Figure 1 shows the course of the disease over the entire period of observation on the basis of the mean value of the symptoms index.

For the first part of the treatment period (days 0 to 8), a rapid improvement in the symptoms was noted **(Table 3)**. A total of 72% of the patients became symptom-free within the treatment period (days 0–14).

Assessment of the symptoms was carried out using the rank scale system, with scores of 0 to 1 being assigned to the symptoms drowsiness and nausea, while the remaining symptoms were given scores of between 0 and 3.

Subjective overall assessment of the course of the illness during treatment (results of treatment)

The efficacy of Echinaforce was assessed to be clinically relevant by 88.2% of the patients themselves, and in 86.8% of the cases by the care-providing physicians **(Figure 2)**.

Tolerability

During the period of treatment with Echinaforce, totalling 1,068 patient days, 97.3% of the patients assessed tolerability to be good. The assessment «good» by the care-providing physicians was an even higher 98.7% **(Figure 3)**.

Only in one of the 77 participating patients did undesirable side effects that led to the abandonment of the test medication by the patient occur, namely on the fourth day of use, when he experienced nausea, a subjective feeling of restlessness, and aggravation of the overall symptomatology.

Discussion

The present study demonstrates the efficacy of Echinaforce drops used to improve the symptomatology of upper respiratory infection, on the basis of a consideration of the course of the illness and the condition of the patient.

The clinical findings, evaluated on the basis of a symptoms index, improved appreciably during the period of observation. A mean value of 0.45 at the end of the period of observation (maximum symptoms index: 35) represents virtually complete healing of the upper respiratory infection. In addition, the therapeutic efficacy was also clinically relevant in 80% of the cases, as shown by the subjective assessment of both physicians and patients.

Indeed, tolerability was considered by both physicians and patients to be good in more than 97% of the cases.

Thus, in the present study Echinaforce has proved to be a highly

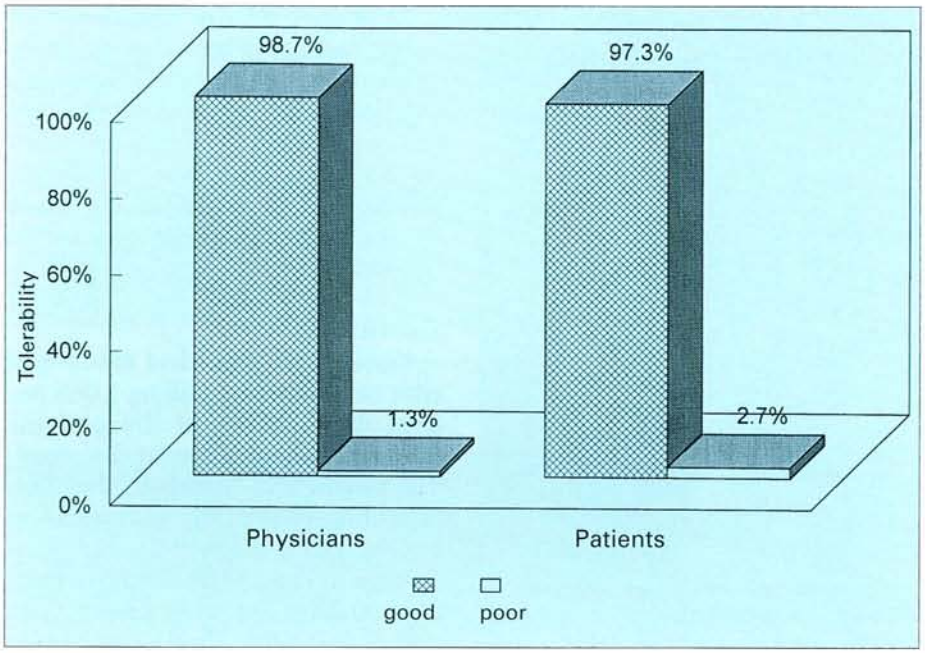

Figure 3: Subjective overall tolerability of Echinaforce in the view of the patients and care-providing physicians. The positive assessment of tolerability (very good, good, satisfactory) was represented as well tolerated; the negative assessment (very little, poor, none) as poorly tolerated. A total of 77 patients were assessed.

effective form of symptomatological treatment of upper respiratory infection, and has shown excellent tolerability.

In accordance with the present state of our knowledge, therefore, Echinaforce can be employed with a very good chance of success in the prophylaxis and treatment of recurrent infections.

Conclusions

The present clinical study shows that Echinaforce is capable of eliminating the symptoms of upper respiratory infections, and also that it is very well tolerated.

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