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Echinaforce® in the treatment of acute colds

Results of a placebo-controlled double-blind study carried out in Sweden

Echinaforce® is a fresh-plant preparation obtained by aqueous-alcoholic extraction from the aerial parts (95%) and roots (5%) of *Echinacea purpurea* (coneflower). The preparation is available commercially in the form of drops and tablets. Its efficacy in the treatment of acute colds has long been known, and has now been invesigated in a placebo-controlled, double-blind study carried out in Sweden. Treatment with a daily dose of 3×2 tablets over a period of 8 days resulted in a clearly greater reduction in clinical symptoms than that seen with placebo, in a total of 119 patients, some of whom used additional medication directed against cold. In the estimation of the examining physician, the test substance was effective in 68%, and in the estimation of the patients in 78%, of the cases. Tolerability was reported to be good in more than 95% of the cases. Adverse events possibly associated with Echinaforce® were comparably as rare as with placebo, and mild to – in one case – moderate.

Colds occur mainly in the winter and are caused by viral infections. For the most part, the usual treatment with nose drops, hot drinks and a vitamin-rich diet leads merely to a brief reduction or elimination of symptoms. Although a number of earlier clinical trials with other preparations containing *Echinacea purpurea* provided evidence of its efficacy in the treatment of colds, in the opinion of the authors of a review, they did not suffice to warrant unequivocal recommendations with respect to dosage and form of application [1].

Echinaforce is a preparation obtained exclusively from *Echinacea purpurea* (coneflower) by aqueous-alcoholic extraction, and comprises 95% aerial parts and 5% roots of the freshly harvested plant. The plants are obtained from controlled biological cultivation at suitable sites, are grown from the producer's own seeds, and are harvested by hand. The preparation has been used for years in the treatment and prevention of acute colds, and statements by numerous patients bear testimony to its effectiveness.

The following constituent substances have been isolated: alkylamides, chicoric acid, polysaccharides, glycoproteins, flavonoids and essential oil.

In vitro investigations show an inhibitory effect on inflammation and on the growth of bacteria, viruses and fungi, which present knowledge shows to be based on the stimulation of controlling elements of our immune system, leading, for example, to an increase in polymorphonuclear leukocytes and natural killer cells, and thus to an increase in phagocytic activity [2].

In a multi-centre clinical observational trial involving 77 patients with influenza-like infection, carried out between September 1989 and April 1990 in Austria, treatment with 3 × 30 drops of Echinaforce daily was applied for a period of 14 days. On the basis of the observations of the examining physicians and their patients, a clinically relevant improvement in the symptoms associated with this illness was noted. 76 of the patients assessed tolerability to be good. Adverse events occurred in only a single patient in the form of restlessness and a worsening of the overall clinical symptoms with onset on the first day (of treatment) leading to discontinuation of treatment on day four. The causal relationship of these events to Echi-

naforce was questioned by the examining physician, who considered it quite unlikely, since he had often observed such events in this patient on earlier occasions [3].

Aim and design of the study

The following results represent a preliminary report of a placebo-controlled trial with an Echinaforce arm and two other treatment arms and employing the tablet form, a more detailed report of which will later be published elsewhere. The trial was carried out under the direction of Dr. R. Brinkeborn, a specialist for infectious diseases at a hospital in Uppsala (Sweden). The infection-prone test subjects were recruited in the autumn of 1996 via newspaper advertisements. On the occasion of their first visit to the hospital, the test subjects were given their medication on a random allocation basis and were instructed to begin taking it immediately following the onset of the symptoms of a cold, and then to return to the hospital on the same or the next day (second visit). The purpose of the third and last visit was to perform a final examination after recovery, or at the latest on the 8th day of treatment. The period of observation for all test subjects extended from the end of November 1996 to the end of May, 1997.

Treatment comprised a daily dose of 3 × 2 tablets of Echinaforce, each containing 6.78 mg *Echinacea purpurea*, native extract, (DEV = 5.9:1), or the same number of inactive placebo tablets of identical appearance.

The following 12 symptoms were employed as efficacy parameters, each of which was given a score by the physician and the patient of between 0 and 3 points (absent, mild, moderate, severe):

1. Overall clinical picture
2. Nasal catarrh, running nose
3. Watering or a «burning» sensation affecting the eyes
4. Sore throat and difficulty in swallowing
5. Headache and dizziness
6. Drowsiness and lassitude
7. Muscular and limb pain
8. Fever
9. Cough
10. Stuffy nose
11. Earache
12. Other cold-related symptoms

The results were used to calculate a summed score that served as a symptoms index for each individual patient. Statistical analysis was carried out using the one-sided U-test.

	Treatment	n	Index visit 2	Index visit 3	Relative reduction	One-sided U-test vs. placebo
ITT	Echinaforce	55	9.0 ± 4.2	4.1 ± 4.5	59% ± 36%	p = 0.045
	Placebo	64	8.8 ± 3.7	5.3 ± 5.1	34% ± 68%	
PP	Echinaforce	41	8.8 ± 3.4	3.5 ± 4.0	63% ± 34%	p = 0.007
	Placebo	46	8.3 ± 3.4	5.6 ± 4.9	29% ± 61%	

ITT = intention-to-treat analysis
PP = per-protocol analysis

Table 1: Symptoms index and relative reduction of 12 cold symptoms (mean values ± standard deviations).

Results

During the period under observation, 66 of the subjects who became ill were assigned to treatment with Echinaforce, and 64 to the placebo group. Thirteen of the patients in the former group, and 17 patients in the placebo group also used additional medication aimed at relieving cold-related symptoms, such as nose drops or antipyretic medication containing paracetamol. In addition, one patient dropped out of the placebo group, while one of the patients in the preparation group started treatment too late. To ensure a complete picture of the therapeutic efficacy of Echinaforce in acute colds, therefore, both the overall population – in the intention-to-treat analysis – and the group of patients complying with the protocol, i.e. excluding those employing impermissible additional medication, drop outs and those delaying treatment initiation – in the per-protocol analysis – were compared with the respective placebo groups.

Efficacy

The decisive parameter for assessing therapeutic success was the relative reduction in the symptoms index. In comparison with placebo, Echinaforce proved to be clinically relevantly – and in the per-protocol analysis very significantly – superior. **Table 1** shows the means and standard deviations of the symptoms indices and their relative reduction.

Furthermore, as can be seen in **Figures 1** and **2**, the high level of efficacy of the preparation in comparison with placebo was confirmed by the percentage estimations by the physician and the patient (z-test $p<0.005$).

Tolerability

Tolerability was assessed to be good by the examining physician in 98% of the cases, and by the patients in 96% of the cases.

The five adverse events observed under Echinaforce and having a possible or likely causal link were – with the exception of one patient who had moderate symptoms – mild in nature, and took the form of gastrointestinal symptoms such as nausea or upper abdominal dis-

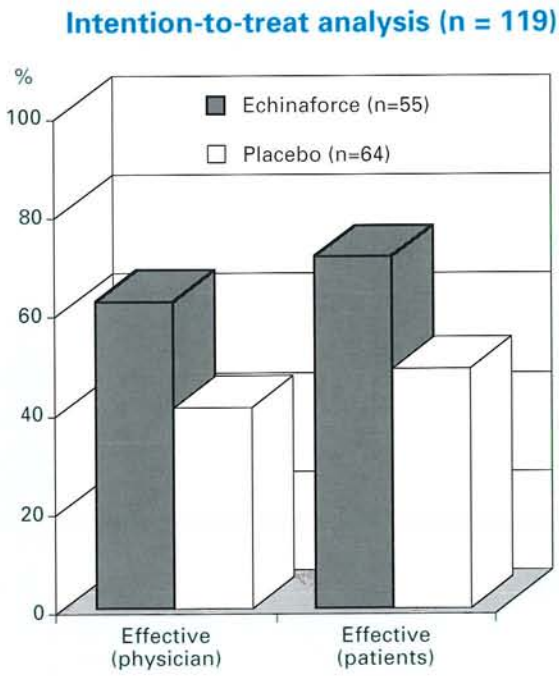

Figure 1: Assessment of efficacy (intention-to-treat analysis, n = 119).

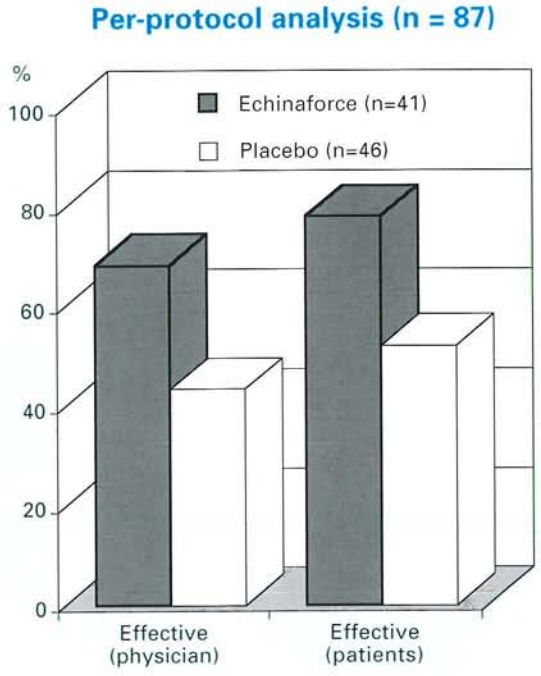

Figure 2: Assessment of efficacy (per-protocol analysis, n = 87).

Severity	Causality	Echinaforce	Placebo
moderate	possible	1 gastrointestinal	
mild	likely or possible	4 gastrointestinal	3 gastrointestinal 1 nervous system
mild	unlikely	1 gastrointestinal 1 general	1 gastrointestinal 1 cutaneous

Table 2. Undesired events: severity, causal relationship, organs.

comfort or sleep disorders. Such adverse events also occurred in the placebo group **(Table 2)**.

Summary

The findings presented here indicate that, in the acute treatment of colds, Echinaforce is clearly superior to placebo in terms of efficacy, and its tolerability is comparably good. Thus, this preparation may be recommended as well suited to the treatment of colds in the acute stage.

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