SECRETOLYSIS AND BRONCHOSPASMOLYSIS

CURRENT PHARMACEUTICAL TOPICS **FOCUS**

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The effects of the ingredients of dried ivy leaf extract (Hederae helicis folium) have been used therapeutically as an expectorant since ancient times. The purpose of prescribing expectorants is to prevent or eliminate mucostasis and ideally to reduce the relapse rate of infections.

Increase in mucociliary clearance

The pathophysiological process of mucostasis is characterised by multifactorial causes. Effective elimination of mucus can be achieved by increasing mucociliary clearance, liquefying mucus and hence improving cough function with different drugs.

The efficacy of dried ivy leaf extract has been acknowledged by the German supervisory authorities in the positive-list monograph and the licence for Prospan® drops in the indications of "coughs, colds affecting the respiratory tract and improvement of disorders in chronic inflammatory bronchial diseases," but not including the suppository dosage form.

Clinical studies in patients with chronic inflammatory bronchial diseases, such as bronchial asthma, are suitable for comparing the efficacy of different presentations, such as suppositories and drops. A validated method of demonstrating efficacy is offered by pulmonary function diagnosis using body plethysmography and spirometry, by which the secretolytic and bronchospasmolytic effect of dried ivy leaf extract can be demonstrated in respect of improvements in ventilatory disorders.

Study design

In the case of therapy with suppositories for children, it should be borne in mind that they are generally accepted by children only over a short period of time.

Accordingly, the shortest possible period was chosen in the clinical study to compare the efficacy of the suppository and drops dosage forms.

Clinical experience has shown that the secretolytic and bronchospasmolytic effect after treatment with dried ivy leaf extract occurs after a short time, so that a treatment period of 3 days may be considered clinically suitable. The efficacy and tolerability of dried ivy leaf extract children's suppositories and dried ivy leaf extract drops was to be compared in a randomised cross-over study in children with chronic obstructive airways disease.

Patients/Methodology

The criteria of inclusion in the study comprised the signature of the declaration of consent by the parents or guardians, the diagnosis of "chronic obstructive airways disease" and an at least 10% reversibility of the bronchial obstruction. This was measured by determining the forced expiratory volume in 1 second without medication and 10 minutes after inhalation of 200 µg fenoterol and demonstrating an increase of at least 10%. Criteria of exclusion from the study comprised an airways resistance of > 0.9 (kPa/l/s), age< 4 and > 12 years and concomitant antibiotic therapy.

Dried ivy leaf extract suppositories for children and dried ivy leaf extract drops were administered as test substances. 100 ml of drops contained 2.00 g and 1 children's suppository contains 80 mg of standardised dried ivy leaf extract (5-7.5:1). In accordance with the manufacturers instructions, the children received 1 dried ivy leaf extract suppository twice daily for three days throughout the course of the study or 25 dried ivy leaf extract drops at 7.00 am and 7.00 pm according to the randomisation plan, following a wash-out phase of 2 to 4 days when administration of inhalational $ß_2$ -mimetics was permitted. The daily dose after administration of the children's suppositories and drops was 160 and 35 mg dried ivy leaf extract, respectively.

After collection of the data, all differential diagnoses of relevance to the study were noted and concurrent diseases documented. Over the whole 8-to 10-day treatment period, the children/parents or guardians were given a peak flow meter and asked to document the peak flow value daily at 7.00 am and 7.00 pm and to assess coughing, dyspnoea and expectoration. Any intolerance of the medication had to be documented in detail.

Airways resistance and the reversibility of bronchial obstruction was determined before the beginning of treatment.

Pulmonary function measurements were taken spirometrically on day 1 of treatment before administration and 3 hours after medication by determining the forced expiratory volume in 1 second (FEV_1), the forced vital capacity (FVC) and the peak flow value (PEF). On day 3 of treatment, in addition to spirometry, the target parameters of airways resistance, intrathoracic gas volume, residual volume and specific airways resistance were determined by body plethysmography.

It was ensured that no inhalational $ß_2$-sympathomimetics had been administered 6 hours before the examination times for the pulmonary function diagnosis and this was noted in the documen-tation forms. It was established at all the pulmonary function measurement times that this was always done at the same time of day and that circadian variations in assessing changes in pulmonary function could be excluded.

The improvements in pulmonary function proved to be clinically relevant and also statistically significant.

Results

The clinical study was undertaken with 26 in-patients (11 girls and 15 boys) with a mean age of 7.2 years (range 5-11 years), a mean