Statistical Evaluation of an Application Study with the preparation series FORTAKEHL

in the administration forms of capsules, tablets, drops, suppositories, injections

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Verlag für experimentelle Onkologie GmbH · 27316 Hoya · Germany

1 Introduction

From June 1995 to December 1999 a total of 97 patients were tested by 10 Doctors practices (7 General Practitioners and 3 Internists) in an observation study with the application of the preparation series Fortakehl in the following administration forms: capsules, tablets, drops, suppositories and solution for injection. The homeopathic test preparation Fortakehl comprising of the third to the fifth decimal dilutions of Penicillium roquefortii, each according to administration dosage.

Fortakehl drops contain Penicillium roquefortii D5 dil. in accordance with Prescription 5a HAB1.

1 ampoule of Fortakehl solution for injection contains 1 ml Penicillium roquefortii D5 aquos. dil. in accordance with Prescription 5b and 11 HAB 1.

1 Fortakehl tablet contains 250 mg Penicillium roquefortii D5 trit. in accordance with Prescription 6 HAB 1.

1 Fortakehl capsule contains: 330 mg Penicillium roquefortii D4 trit. in accordance with Prescription 6 HAB 1.

1 Fortakehl suppository contains: 0.2 g Penicillium roquefortii D3 trit. in accordance with Prescription 6 HAB 1.

The aim of the observation was to establish the actual application of the preparations and their tolerance under conditions in every-day practice, moreover that recognition over the acceptance of the preparations on the market should be gained, in particular with children.

In accordance with the structure of the investigation descriptive statistical procedures were drawn. The application of inductive methods were not indicated. An „intention to treat“ assessment was carried out, i.e. all patients were considered who received at least one dose of the medicament.

2 Participating Patients

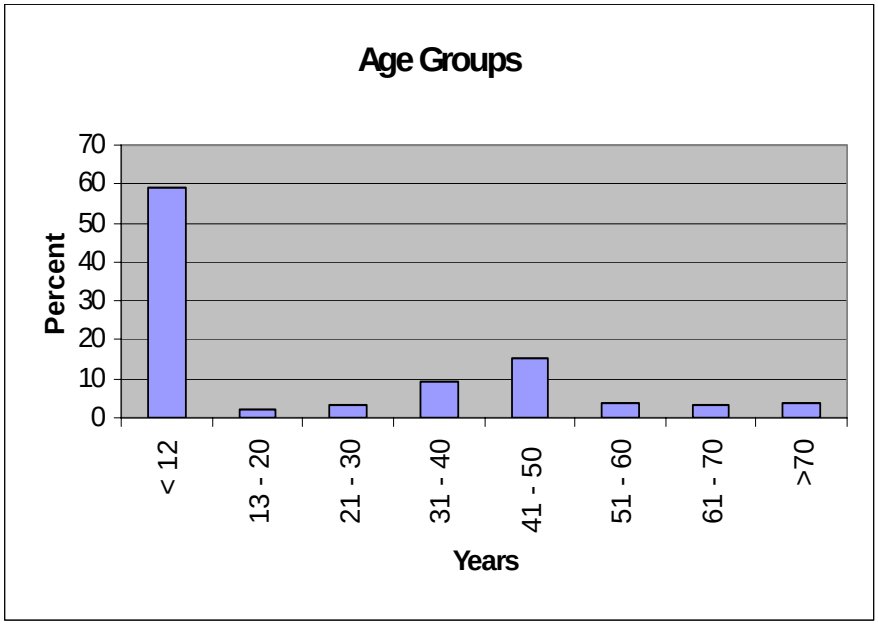
Included in the study were 97 patients, which comprised of 33% men and 67% women. The age of the patients varied between 3 months and 82 years with an average age of 22.4 years and a standard deviation of 22.4 years. Over half the patients (58.8%) were under 12 years of age. Between the ages of 13 and 20 accounted for 2.1% of the patients, between 21 and 30 years, 3.1% and 31 and 40, 9.3%. Apart from the under 12 age group, the age group between 41 and 50 years was the largest with 15.5%. Between 51 to 60 years accounted for 4.1%, 61 to 70, 3.1% and finally, over 71 years made up 4.1% of the patients. The average age structure of the men was 14.4 ± 19.3 approximately 12 years younger than the women with 26.3 ± 22.9 years.

Height varied between 62 and 186 cm with an average of 132.8 ± 36.7 cm. Body weight lay between 5.8 and 115.3 kg with an average of 42.4 ± 26.9 kg.

2.1 Diagnosis and Accompanying Diseases

The diagnosis leading to the prescription was to be entered into the Study protocol. It was herewith set out that Fortakehl, corresponding to Isopathy, in a very wide area of application be applied and the preferred use dependent on the age of the patients.

Whilst Fortakehl was mainly applied in the younger patient groups under 12 years with bronchitis, dermititis atopica and vulnerability to infection, patients in the over 12 age group stood in the



foreground with illnesses such as enteritis, colitis and mycosis.

Collected findings were carried out each before and after completion of the treatment and accompanying therapies were to be documented in a survey form. In order to obtain a measurement of chronic diseases it was asked in the study protocol, how long the disease or discomfort has been in existence. For this a time span of less than 6 months to 1 year, up to 3 years and over 3 years was laid down. The duration of complaints of less than 6 months accounted for 43.5% of patients, 17.6% between 6 and 12 months and 16.5% up to 3 years. Almost a quarter of the patients (22.4%) suffered discomfort for over 36 months. The under 12 age group who had discomfort for less than six months had almost the same percentage (62%) as with the over 12 age groups who suffered discomfort for longer than 36 months. There are no details available for 12 of the patients.

Of the 97 patients included in the study, 23 patients (20 patients < 12 years, 3 patients > 12 years) had previously been treated with Fortakehl.

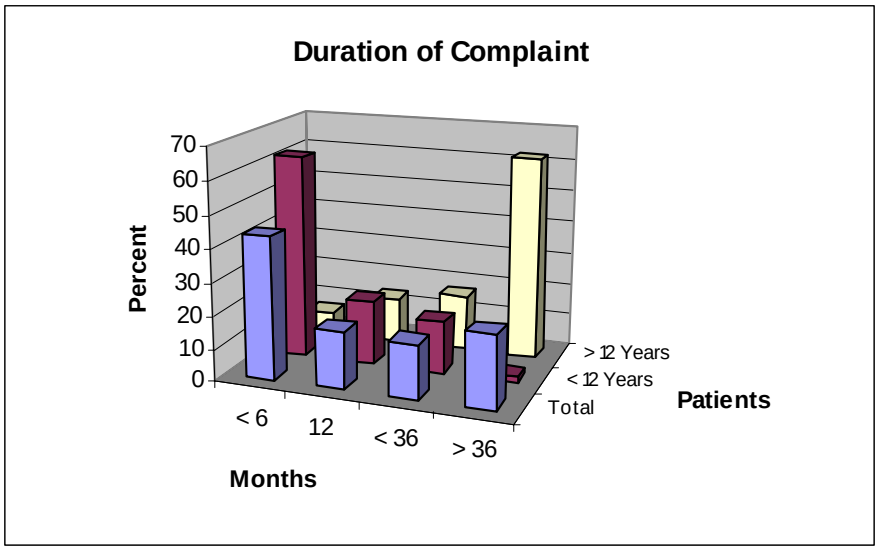
Duration of Complaints (Months)	Total Patient Population (%)	Patients < 12 years (%)	Patients > 12 years (%)
< 6	43.5	62.5	6.9
6 - 12	17.6	19.6	13.8
< 36	16.5	16.1	17.2
> 36	22.4	1.8	62.1

3 Dosage and Duration of Treatment

3.1 Time of Consultation and Duration of Treatment

Corresponding to the nature of application observation no rigid time limit was laid down for a final examination which was carried out in a time span between 1 and 733 days with an average of 63 ± 113 days.

Duration of the therapy in children (< 12 years) was on average 62.3 ± 136 days, just as long as with the adult groups with 64 ± 67.5 days.



The brief therapy of up to 25 days stood in the foreground with 70.7% of the patients under 12 years, whilst with the adults, which made up exactly half of all patients, it was not so strongly pronounced.

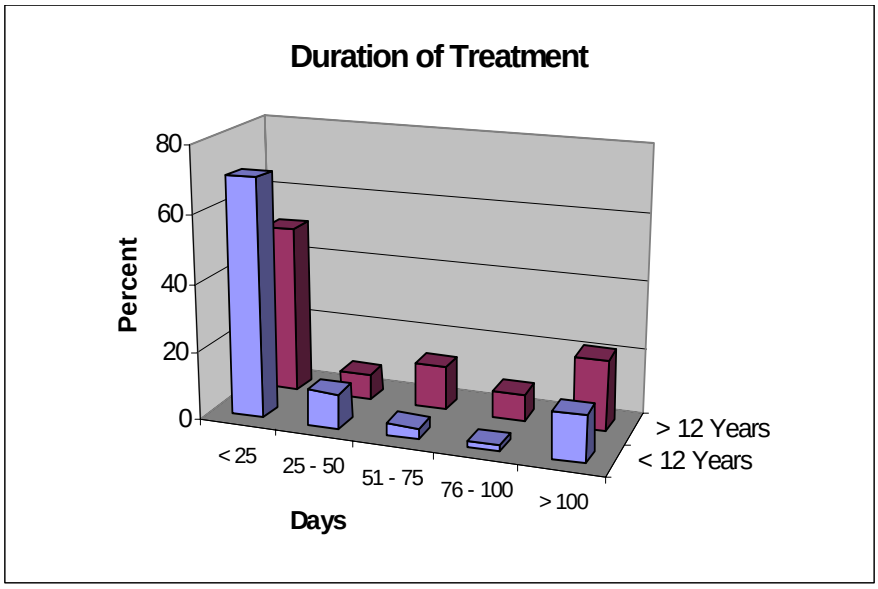
3.2 Dosage

The dosage was prescribed for the relevant form of administration according to the package insert with:

Fortakehl Drops
For oral intake: 1 x 8 drops daily before mealtimes
For inhalation: 2-3 x daily inhale 20-30 drops
For topical application:
a) 1 x daily 5-10 drops at the location of the complaint or massage into the crease of the elbow.
b) By injection treatment; on injection free days 2 x weekly 5-10 drops

Fortakehl Solution for Injection
2 x weekly, inject 1.0 ml either i.m., s.c., i.c., or i.v.

Fortakehl Tablets
Daily 1-3 tablets with some fluid to be taken either after supper or in the morning two hours before breakfast.



Fortakehl Capsules
Daily 1-3 capsules either before breakfast or evenings before bedtime to be taken with some fluid.

Fortakehl Suppositories
1 x daily before bedtime 1 suppository to be inserted rectally.

With reference to the dosage forms, 12 patients were prescribed capsules, 12 patients with tablets, 58 patients with drops for oral intake, 8 patients with drops for topical application, 3 patients with

Dosage			
Total population	**Medium Dose**	**Minimum Dose**	**Maximum Dose**
Capsules	2.1 ± 0.9	1	5
Tablets	1.6 ± 0.9	1	3
Drops (oral)	12.2 ± 8.8	4	30
Drops (topical)	19.1 ± 30.7	3	100
Drops (inhale)	8.0 ± 1.6	6	10
Suppositories	1.0	1	1
Injection (ml)	1.5 ± 0.5	1	2

Dosage				
All patients < 12 years	**Medium Dose**	**Minimum Dose**	**Maximum Dose**	**No. of Patients**
Capsules	2.3	1	1	3
Tablets	1.0	1	1	2
Drops (oral)	8.5 ± 3.9	4	30	44
Drops (topical)	23.8 ± 34.2	3	100	6
Drops (inhale)	8.0 ± 1.6	6	10	3
Suppositories	1.0	1	1	1

Dosage				
All patients > 12 years	**Medium Dose**	**Minimum Dose**	**Maximum Dose**	**No. of Patients**
Capsules	2.3 ± 0.8	2	5	12
Tablets	1.7 ± 0.9	1	3	10
Drops (oral)	23.9 ± 9.7	8	30	14
Drops (topical)	5.0	5	5	2
Suppositories	1.0	1	1	4
Injection (ml)	1.5 ± 0.5	1	2	8

drops for inhalation, 5 patients with suppositories and 8 patients with the solution for injection. Multiple entries were necessary if various administration forms were to be combined. The tables below show the medium dosage with respect to the administration form. Injection volumes were administered for one week and the remaining dosage forms were prescribed to the relevant daily dosage.

Except for the drops, nothing else was substantially administered for the under and over 12 age groups. The dosage of the drops for oral intake is approximately three times as high as with the under 12 age group. The prescribed daily dosage of 30 drops for oral intake for 10 patients in the adult group corresponded to 3.5 times the recommended dosage.

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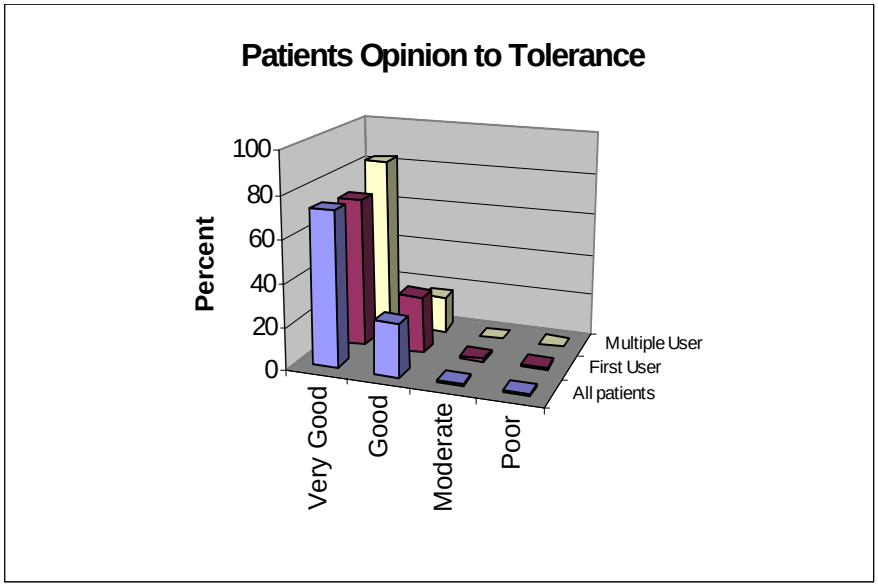
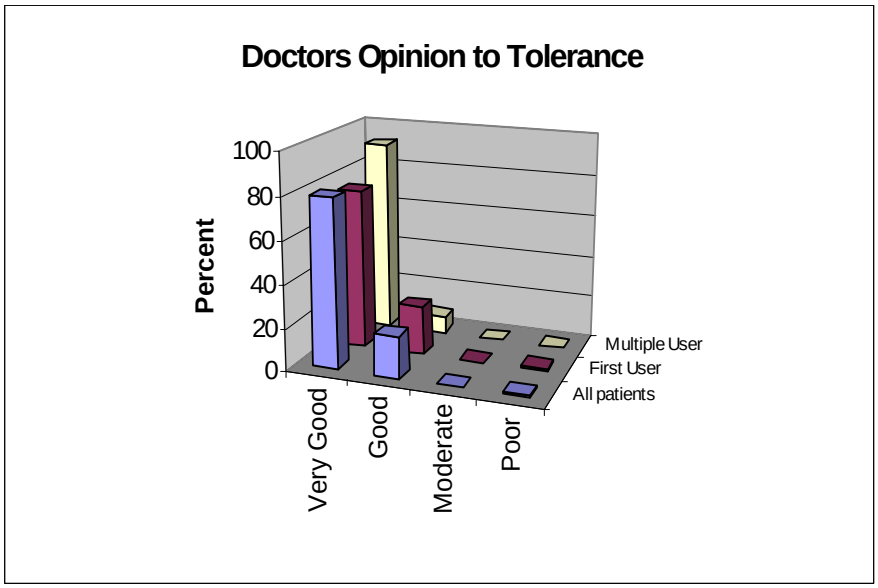
Beside the mono-therapy with one administration form, different administration forms were also combined into the therapy. Because the injection was applied in weekly rotation, 7 patients were prescribed additionaly with capsules, 1 patient, tablets, 3 patients with drops for oral intake and topical application respectively within the injection free time. A combination of more than two dosage forms was not prescribed. There was no difference in the extent of the combination of dosage forms in both age groups as no injections were prescribed, therefore, combination possibilities were not offered. Drops for oral intake and topical application were





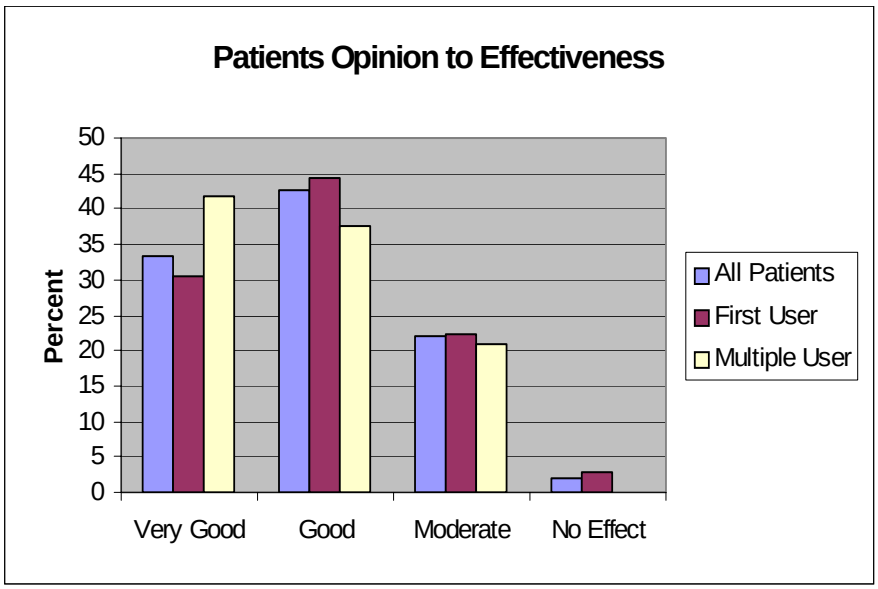
Evaluation of tolerance								
Patient Group	**Patients' evaluation (%)**				**Doctors' evaluation (%)**			
	Very Good	Good	Moderate	Poor	Very Good	Good	Moderate	Poor
All Patients	73.2	24.8	1.0	1.0	79.6	19.4	0	1.0
First User	70.3	27.0	1.3	1.4	75.7	23.0	0	1.3
Multiple User	82.6	17.4	0	0	91.7	8.3	0	0

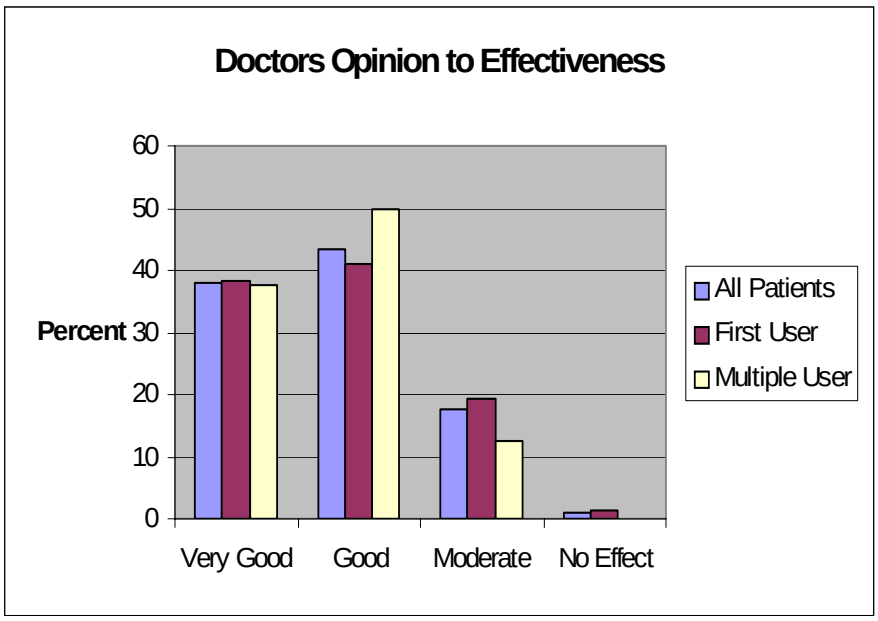
Evalulation of effectiveness								
Patient Group	**Patients' evaluation (%)**				**Doctors' evaluation (%)**			
	Very Good	Good	Moderate	No Effect	Very Good	Good	Moderate	No Effect
All Patients	33.3	42.7	21.9	2.1	38.2	43.3	17.5	1.0
First User	30.6	44.4	22.2	2.8	38.3	41.1	19.2	1.4
Multiple User	41.7	37.5	20.8	0	37.5	50.0	12.5	0

combined in only one case in the under 12 age group.

4 Comparison with Former Therapy

23 patients had already received therapy with one or several administration forms of Fortakehl within the last five years. Since a quarter of the patients had already earlier experienced therapy with Fortakehl, a comparison was to be established as to effectiveness and tolerance in both patient groups of First and Multiple Users with comments of possible tendencies towards sensitisation from the pharmaceutically effective components.





Opinion to tolerance by multiple application was in keeping with the trend better than that of single application usage. The assessment to tolerance in general was clearly changed to „very good" by the Multiple Users. From this data, it shows no potential of an exposure to danger regarding sensitisation to patients through the pharmaceutically effective component of Penicillium roquefortii.

The Multiple Users judged effectiveness in keeping with the trend better in the assessment of „very good" than with the First Users. No Multiple User gave an assessment of „no effect", however, the differences in both groups are not at all significant.

The duration of the therapy distinguishes the Mutliple Users with an average therapy duration of 58.0 ± 145 days which is only negligible with the First Users with 64.6 ± 101 days and the total of all patients with 63 ± 113.5 days.

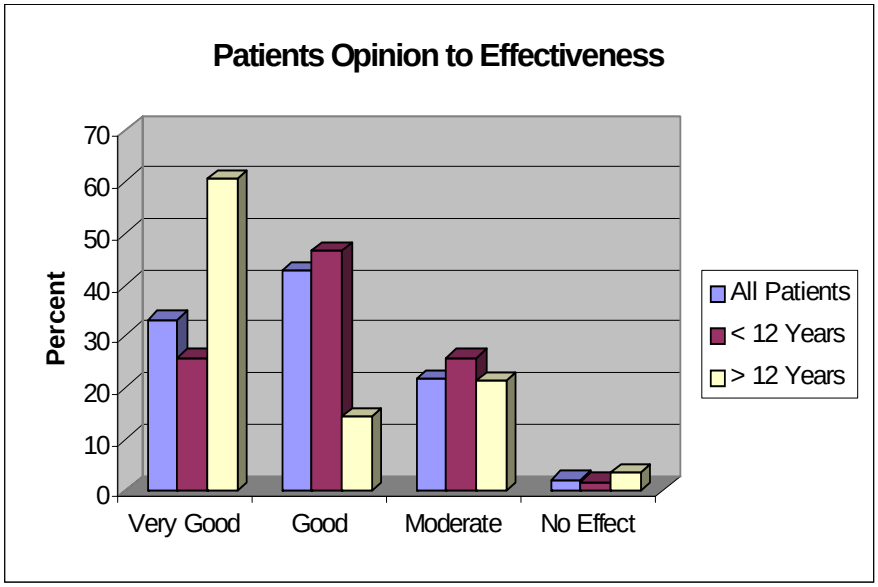
Evalulation of effectiveness								
Patient Group	**Patients' evaluation (%)**				**Doctors' evaluation (%)**			
	Very Good	Good	Moderate	No Effect	Very Good	Good	Moderate	No Effect
All Patients	33.3	42.7	21.9	2.1	38.2	43.3	17.5	1.0
< 12 years	25.9	46.5	25.9	1.7	31.0	41.4	25.9	1.7
> 12 years	60.7	14.3	21.4	3.6	48.7	46.2	5.1	0

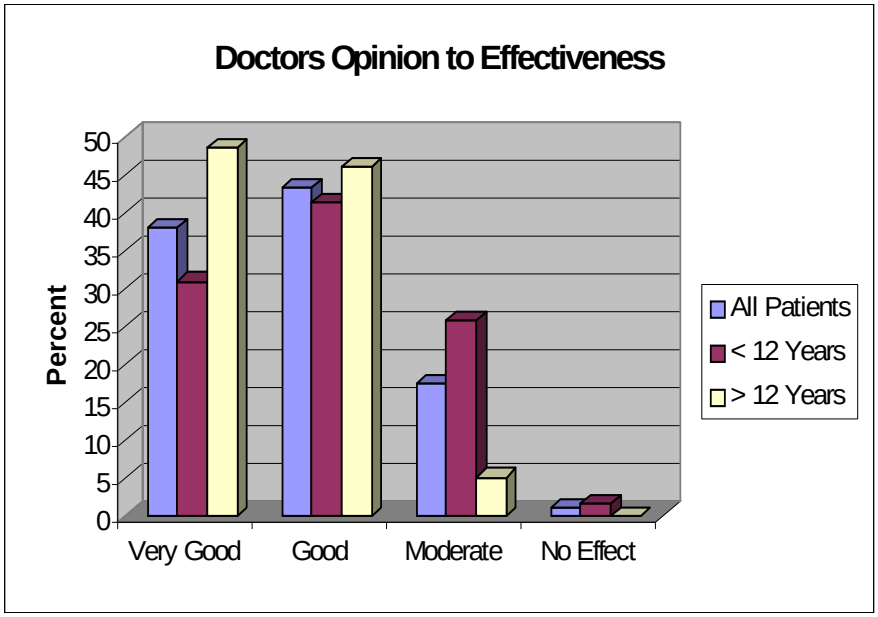
5 Effectiveness and Tolerance

5.1 Assessment of Effectiveness by Doctor and Patient

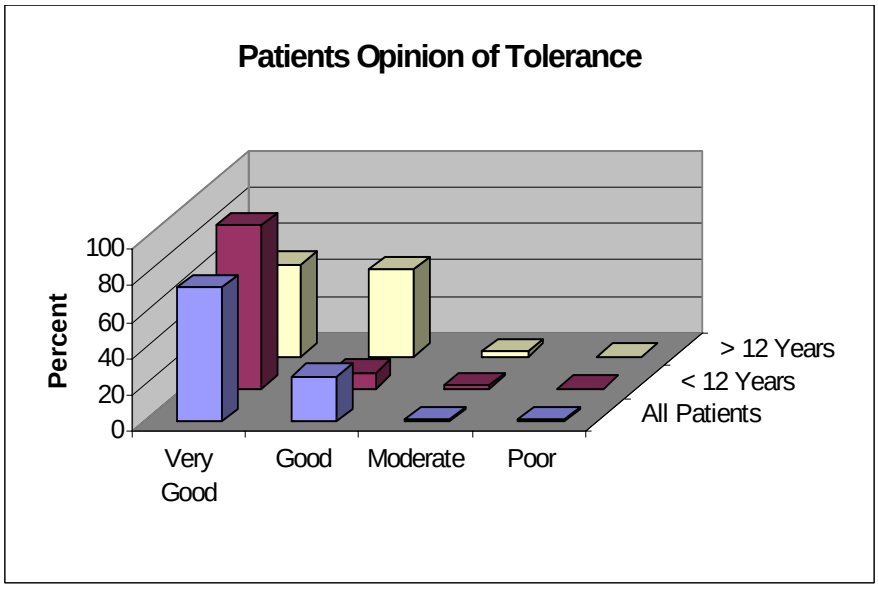
In a final assessment, patients and doctors were asked to assess the effectiveness and tolerance. The effectiveness could be assessed with „very good" „good" „moderate" or „no effect". In addition the doctors were asked according to the patient's compliance to usage, so that it could also be classified with „very good", „good", „moderate" or „poor". 33.3% of patients expressed effectiveness with „very good", 42.7% with „good" whilst 21.9% expressed only „moderate" and 2.1% with „no effect". The doctors assessment to effectiveness was just as positive as with the patients. 38.1% of patients were classified with „very good", 43.3% with „good", 17.5% with „moderate" and 1.0% with „no effect".

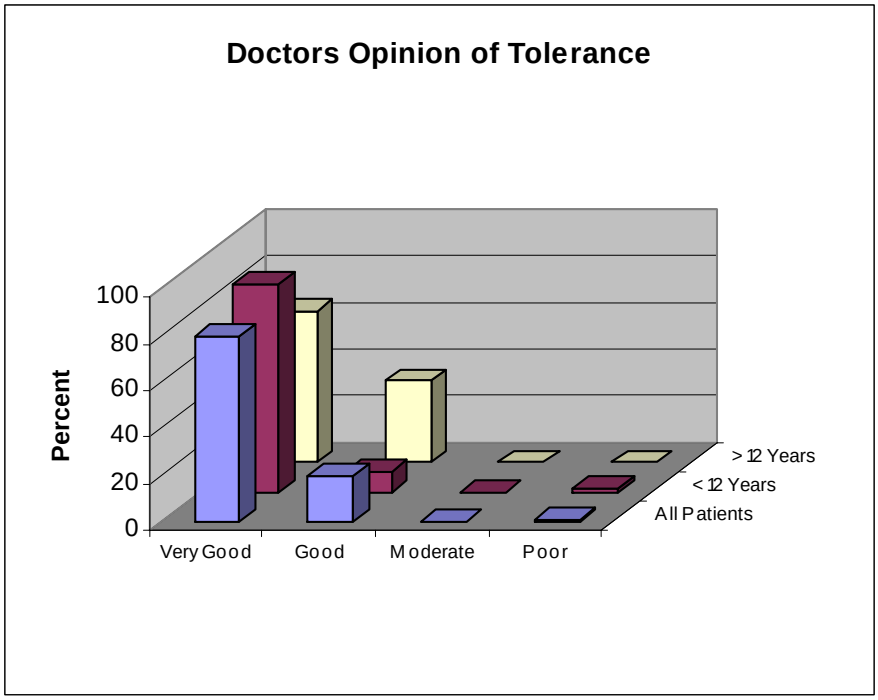
Application behaviour (N=90) was judged by 68 patients with „very good" and „good" by 17 patients





Evaluation of tolerance								
Patient Group	**Patients' evaluation (%)**				**Doctors' evaluation (%)**			
	Very Good	Good	Moderate	Poor	Very Good	Good	Moderate	Poor
All Patients	73.3	24.7	1.0	1.0	79.6	19.4	0	1.0
< 12 years	89.5	8.8	1.7	0	89.7	8.6	0	1.7
> 12 years	50.0	47.5	2.5	0	65.0	35.0	0	0





through their doctor. With it, 87.6% of all those patients involved in the study confirmed „very good“ and „good“ compliance each. For 5 patients, this was only „moderate“ and „poor“ for none of the patients.

5.2 Opinion of Tolerance by Doctor and Patient

To conclude the examination, an assessment to tolerance was submitted from doctors and patients whereby a judgement of „very good“, „good“, „moderate“ and „poor“ could be chosen. 73.3% of patients and 79.6% of doctors classified the tolerance with „very good“ whilst 24.7% of patients and 19.4% of doctors confirmed a good tolerance with Fortakehl.
„Moderate“ tolerance was given by 1.0% of patients and „poor“ tolerance by 1% of patients and doctors respectively.

Tolerance was by far more positively assessed by doctors and patients in the under 12 age group than with the over 12 age group. Whilst in the younger age groups 89% of the patients and doctors indicated tolerance with „very good“, this was with the over 12's only 50% of patients and 65% of doctors. No assessment of „poor“ in the over 12 age group was given by doctors or patients.

5.3 Side Effects and Discontinuation of the Therapy

The therapy with Fortakehl was not discontinued by any of the patients. However 4 cases of side effects were reported which are more closely interpreted as follows: In 1 case, a typical homeopathic primary deterioration was reported by a 49 year old female patient who developed a mycosis of the skin after oral application of 10 drops. A side effect of „coughing“ was given with a four year old girl who was being treated for angina tonsillaris. A four year old boy who received drops for oral intake for enteritis contracted conjunctivitis after the 6th day of treatment. A 2 year old child received 4 drops daily orally for intestinal colic and after two days developed a skin eruption on both lower legs which lasted one week. A connection with the Fortakehl therapy can only be seen from the homeopathic primary deterioration and the last named case of the 2 year old girl. The question remains as to whether both the other cases are connected with Fortakehl. There was one case of local irritation at the point of needle insertion which disappeared again without any further therapy. With the other therapy forms, one patient reported „vomiting, diarrhoea,

tenesmen and fatigue", however, a connection with the Fortakehl therapy did not exist.

In total, no extreme dominant reactions appeared. All those side effects reported were completely reversible.

6 Summary

From June 1995 to December 1999 a total of 97 patients were tested by 10 Doctors practices (7 General Practitioners and 3 Internists) in an observation study with the application of the preparation series Fortakehl in the following administration forms: capsules, tablets, drops, suppositories and solution for injection. The homeopathic test preparation Fortakehl comprising of the third to the fifth decimal dilutions of Penicillium roquefortii, each according to administration dosage. The age of the patients varied between 3 months and 82 years. Almost half of the patients were under 12 years of age.

Fortakehl was applied according to isopathy in a very broad area of application, whereby the preferred use was dependent on the age of the patients. In the younger patient groups under 12 years, Fortakehl was mainly applied with occurrences such as bronchitis, dermatitis atopica and vulnerability to infection. In the over 12 age group diseases such as enteritis, colitis and mycosis were predominant. Accompanying therapies were to be documented in the survey form.

The duration of the therapy for children (<12 years) was on average 91.8 ± 98.6 days, almost a third longer than the adults with 66.5 ± 76.4 days.

Progress of the treatment was in each case determined at the beginning and end of the therapy.

76% of the patients and 81,4% of the doctors described the effects of the treatment as „very good" and „good". Tolerance was judged by 98% of the patients and 99% doctors each as „very good" and „good". There was no break in the study. Side effects and intolerance was documented and these were mostly all without additional therapy and completely reversible. A connection with the Fortakehl therapy could only be made in 1 case causing irritation at the point of needle insertion. One case of homeopathic primary deterioration occurred. Tolerance in the under 12 age group was substantially more positively judged as with the over 12 age group by the doctors as well as the patients.

First published in the German language in the SANUM-Post magazine (61/ 2002)