Statistical Evaluation

of an Application Study with the Preparation Series

Pefrakehl

in the administration forms:
capsules, drops, suppositories, ointment and injections

by Dr. Reiner Heidl
June 2001

Semmelweis-Institut GmbH
Verlag für experimentelle Onkologie GmbH · 27316 Hoya · Germany

1 Introduction

A total number of 142 patients in 11 medical practices, three specialising in internal medicine, seven in general medicine and 1 in ENT, participated between July 1993 and November 1999 in an application study with the preparation series PEFRAKEHL in the administration forms capsules, drops, suppositories, ointment and injections. The homoeopathic test preparation, PEFRAKEHL, consists with respect to the different administration forms, of Candida parapsilosis in the 3rd to 6th decimal potency.

PEFRAKEHL drops contain exclusively Candida parapsilosis D5 dil. in accordance with provision 5a, HAB.
1 ampoule PEFRAKEHL dilution for injection contains: 1 ml Candida parapsilosis D6 aqueous dilution in accordance with provision 5b and 11, HAB.
1 PEFRAKEHL capsule contains: 330 mg Candida parapsilosis D4 trit. in accordance with provision 6, HAB.
1 PEFRAKEHL suppository contains: 0.2 g Candida parapsilosis D3 trit. in accordance with provision 6, HAB.
1 g PEFRAKEHL ointment contains: 0.1 g Candida parapsilosis D3 dil. in accordance with provision 5a, HAB.

The aim of this application study was to determine the actual application of the preparation as well as its tolerance under the day-to-day conditions of a normal practice. It was also of importance to determine the acceptance of the preparation on the market, especially amongst children.

In line with the study's set-up, only descriptive statistical methods were used. The application of inductive methods was not indicated. An „intention-to-treat" evaluation was carried out, which means that all those patients who had at least received one dosage of the medicament were included in the study.

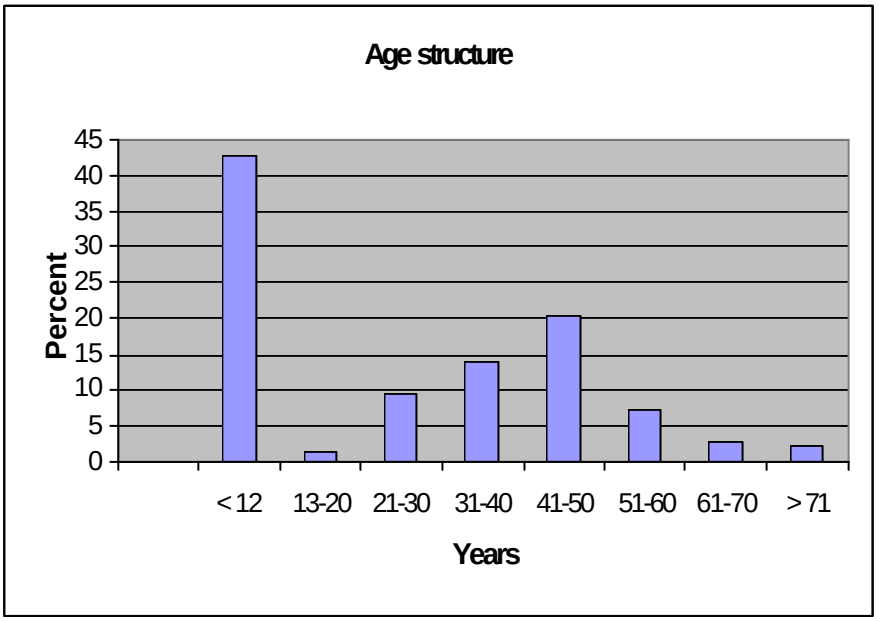
2 Participating Patients

142 patients participated in the study which comprised of 31% males and 69% females. The age of the patients varied between 3 and 80 years, with an average age of 27.0 and a standard deviation of 20.8 years. 42.8% of the patients were under 12 and 1.4% between 13 and 20 years. The age group between 21 and 30 accounted for 9.4% and 13.8% between 31 and 40 years. The second largest age group was the one between 41 and 50 years (20.3%). 7.2% of all patients were between 51 and 60 were, 2.9% between 61 and 70 and 2.2% over 70 years. Regarding age structure, the males with an average age between 24.3 ± 21.8 were on average 4 years younger than the females with 28.2 ± 20.2 years.

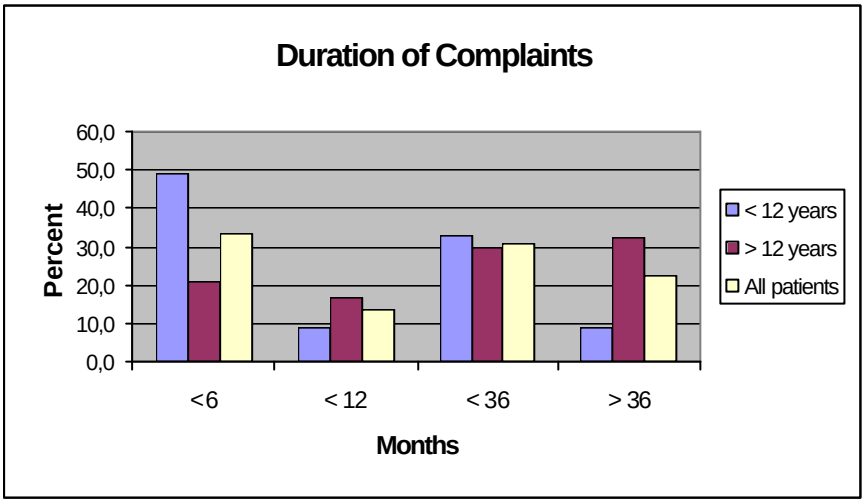
Height varied between 62 and 186 cm with an average height of 145.5 ± 33.3 cm and weight was between 5.8 and 115 kg with an average weight of 50.6 ± 25.6 kg.

2.1 Diagnoses and Secondary Diseases

The diagnosis leading to the prescription was to be entered in the study protocol. It showed that PEFRAKEHL, according to Isopathy, is used in a very wide application range. The preferred application was independent of the patient's age. The main indications were intestinal and skin mykoses. In the age group under 12 years PERAKEHL was also applied with bronchitis, rhinitis, angina and Otitis media. A diagnosis was made



Duration of Complaints (Months)	Patients < 12 years (%)	Patients > 12 years (%)	Total Patient Population (%)
< 6	49.1	21.1	33.3
6-12	9.1	16.9	13.5
< 36	32.7	29.6	31.0
> 36	9.1	32.4	22.2



before the start and end of the therapy. Accompanying therapies were to be documented in the evaluation form.

In order to obtain a measure of chronic diseases, the patients were asked in the study protocol how long they had suffered the disease or complaints. Time frames were given of less than six months, up to one year, up to three years and more than three years.

33.3% of the patients suffered for less than six months, 13.5% between six and 12 months, 31.0% between one and three years and 22.2% for more than three years. A comparison between the patient groups under 12 and over 12 years revealed that almost half of the children under 12 (49.1%) suffered for less than six months and approximately one third of this age group suffered between one and three years. In the adult group over 12 years, chronic complaints between one and three years (29.6%) and over three years (32.4%) were predominant.

30 patients (28 patients < 12 and 2 patients > 12) of the 142 patients included in the study had already been previously treated with PEFRAKEHL.

3. Dosage and Therapy Duration

3.1. Consultation Times, Therapy Duration

According to the nature of an application study, the physicians were not given a preset time limit for the final patient assessment. The final examinations were conducted after a period of 3 to 733 days, with an average of 77 ± 88 days.

The therapy duration amongst the children (< 12 years) was on average 69.0 ± 110.3 days and was only 12 days shorter than the adult group (> 12 years) with 81.7 ± 67.7 days. This significance was to be expected more clearly, as with the age group under 12 years, acute conditions with 25 therapy days at the longest was predominant in 48.2% of the patients, whilst in the group over 12 years this was only the case in 27.2% of the patients. The accumulation of the therapy duration of 75 up to 100 days in the adult group was significant in more than one third of the patients (35.8%).

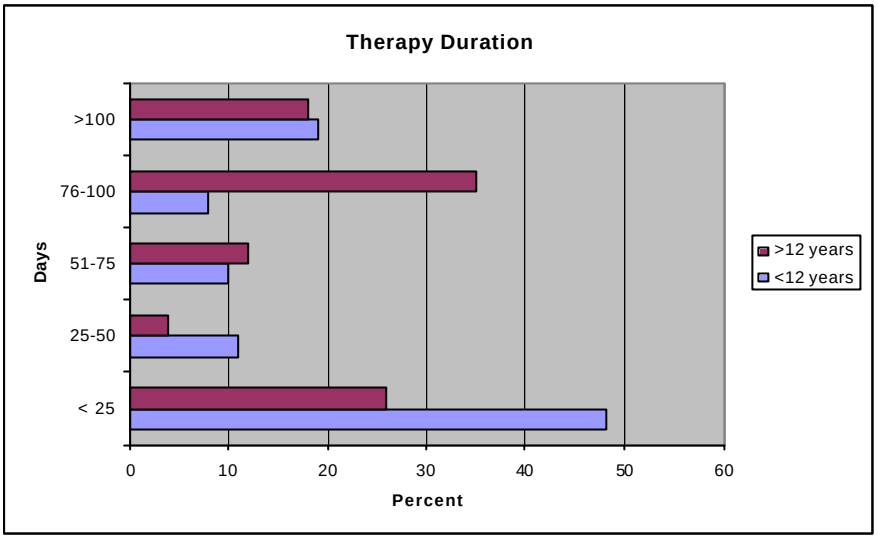
3.2 Dosage

The dosage was set as follows, according to the patient information leaflet:

PEFRAKEHL drops
Oral application: 1x 8 drops daily before a meal.
For inhalation: Inhale deeply 20 - 30x, 2 - 3x daily
Topical application:
a) 1x daily, 5 - 10 drops on the affected area or in the cubital fossa.
b) In case of simultaneous treatment with injections, rub in 2x weekly 5 - 10 drops on injection-free days.

PEFRAKEHL injections
2x weekly 1.0 ml i.m., s.c., i.c. or i.v.

PEFRAKEHL capsules
1 - 3 capsules daily with some liquid before breakfast or in the evenings before going to bed.



PEFRAKEHL suppositories
1x daily, insert 1 suppository rectally at bedtime.

PEFRAKEHL ointment
1 - 3x daily, to be applied in a thin layer on the affected area or in a thick layer onto the dressing.

With respect to the administration forms, 55 patients took capsules, 46 patients were treated orally, 12 patients topically, 3 patients with inhalation, 12 patients with suppositories, 50 patients with ointment and 18 patients with injections. Multiple counts were necessary, if various application forms were combined. The following tables show the average dosage of the administration forms. The injection volumes are related to a weekly dosage and the remaining administration forms to a daily dose.

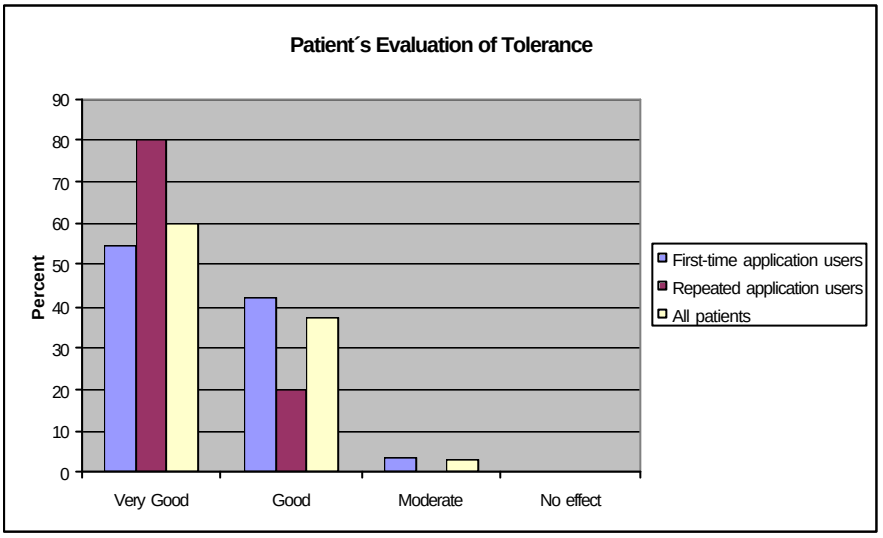
There was no significant difference in the dosages in the age groups under 12 and over 12 years. Besides the monotherapy with one application form, two or three application forms were also combined in the therapy. The combination of injections with the other application forms was predominant in the age group over 12 years. In 16 patients, injections were combined with capsules and in 3 patients with the application of ointment. Two patients were treated with capsules and suppositories and 10 patients with capsules and ointment. In two patients, inhalation was combined with ointment and in two patients topical application with drops for oral intake. No injections were administered in the patient group under 12 years. One patient each received one of the following combination preparations: drops for inhalation were combined with ointment, suppositories with drops for oral intake and drops for topical application with suppositories as well as ointment. The combination of ointment and suppositories and ointment with drops for topical application were prescribed for two patients each. Four patients were treated with drops for topical application combined with suppositories and 10 patients with ointment and capsules. Hence combinations were made to a similar degree in both age groups. A combination of various administration forms of PEFRAKEHL was applied in 36% of the children and in 41% of the adults.

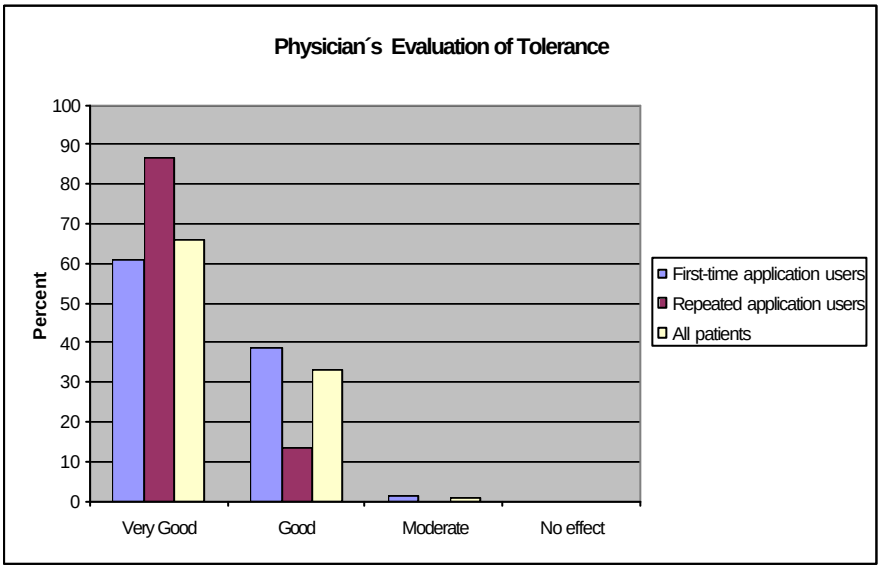
Total Population			
	medium dose	minimum dose	maxiumum dose
Capsules	1.7 ± 0.8	1	3
Drops für oral intake	7.8 ± 1.8	4	10
Drops for topical application	4.0	6	10
Drops for inhalation	5.3 ± 2.0	3	8
Suppositories	1.0	1	1
Ointment (cm)	2.3 ± 1.7	1	10
Injection ml	1.7 ± 0.5	1	2

All patients under 12 years				
	medium dose	minimum dose	maxiumum dose	patients
Capsules	1.5 ± 0.8	1	3	11
Drops für oral intake	7.2 ± 1.7	4	10	30
Drops for topical application	8.2 ± 1.1	6	10	10
Drops for inhalation	8.0	8	8	1
Suppositories	1.0	1	1	8
Ointment (cm)	2.4 ± 2.0	1	10	20

All patients over 12 years				
	medium dose	minimum dose	maxiumum dose	patients
Capsules	1.7 ± 0.9	1	3	44
Drops für oral intake	9.1 ± 1.4	5	10	16
Drops for topical application	8.0	8	8	2
Drops for inhalation	4.0 ± 1.0	3	5	2
Suppositories	1.0	1	1	4
Ointment (cm)	2.2 ± 1.4	1	6	30
Injection ml	1.7 ± 0.5	1	2	18

Evaluation of Tolerance								
Patient Group	Patient´s evaluation (%)				Physician´s evaluation (%)			
	Very good	Good	Moderate	No effect	Very good	Good	Moderate	No effect
First-time-application users	54,5	42,0	3,5	0	60,7	38,4	0,9	0
Repeated application users	80,0	20,0	0	0	86,7	13,3	0	0
All patients	59,9	37,3	2,8	0	66,2	33,1	0,7	0





4. Comparison with former treatment

30 patients (21%) had already been previously treated with one or more administration forms of PEFRAKEHL in the past five years. By a comparison of efficacy and tolerance in both patient groups of first-time and repeated application users, hints of a possible sensitisation towards the ingredient should be determined.
Repeated application users came off clearly better than first-time application users by a comparison of tolerance. Despite in the group of first-time application users, physician and patient assessed tolerance with „very good“ and „good“, the assessment with „very good“ was clearly predominant in the group of repeated application users. No risk potential regarding sensitisation of the patients by the active ingredient Candida parapsilosis could be derived from the data.

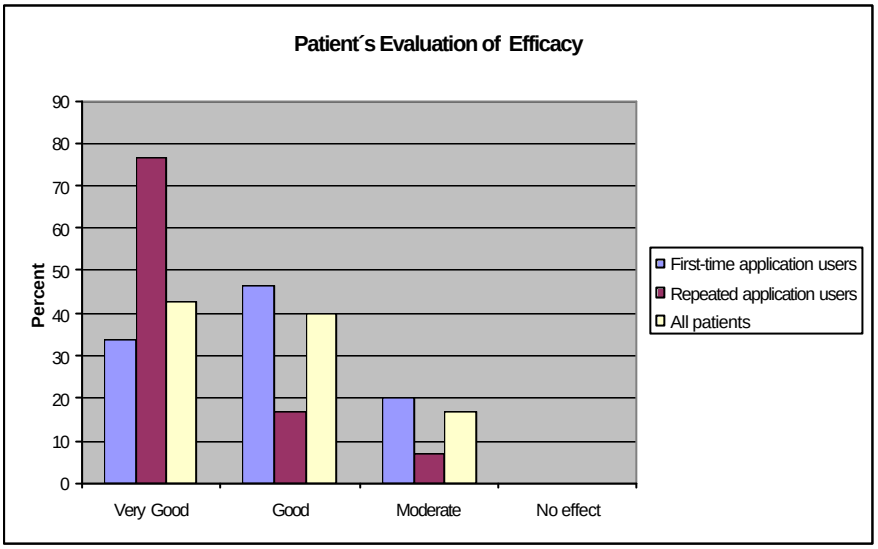
Regarding efficacy, repeated application users were assessed by patients and physicians alike with „very good“ which was twice as many as with first-time application users.
With regard to the therapy duration, repeated application users (on average 66.6 ± 39.0 days) had a therapy duration of 11 days less than the average. First-time application users (80.0 ± 96.8 days) were on average treated 14 days longer.

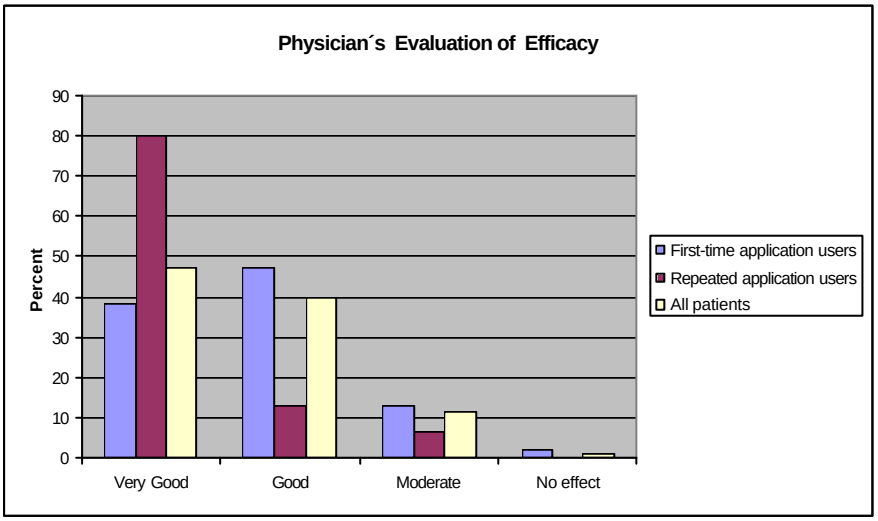
5 Efficacy and tolerance

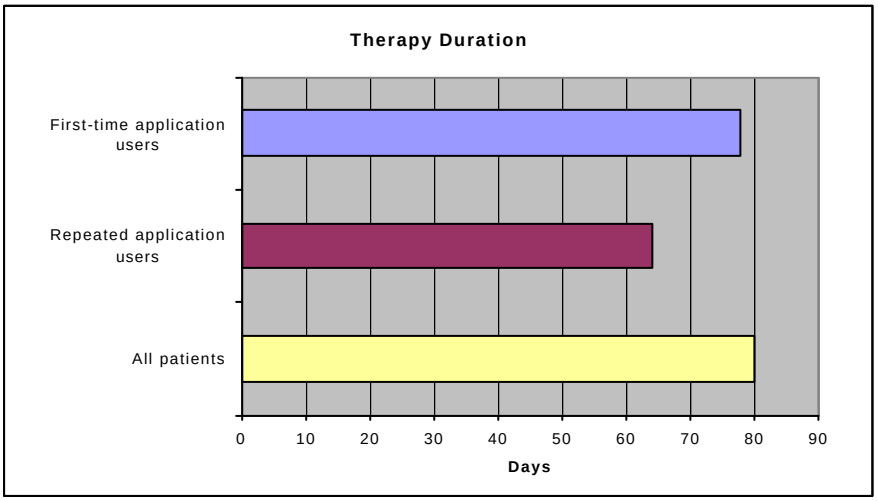
5.1 Evaluation of Efficacy by Physician and Patient

In a closing assessment, physicians and patients were asked to evaluate efficacy and tolerance. Efficacy could be assessed with „very good“, „good“, „moderate“ or „no effect“. The physicians were also requested to evaluate patient

Evaluation of Efficacy								
Patient Group	Patient´s evaluation (%)				Physician´s evaluation (%)			
	Very good	Good	Moderate	No effect	Very good	Good	Moderate	No effect
First-time-application users	33,6	46,4	20,0	0	38,2	47,3	12,7	1,8
Repeated application users	76,7	16,7	6,6	0	80,0	13,3	6,7	0
All patients	42,9	40,0	17,1	0	47,1	40,0	11,5	1,4







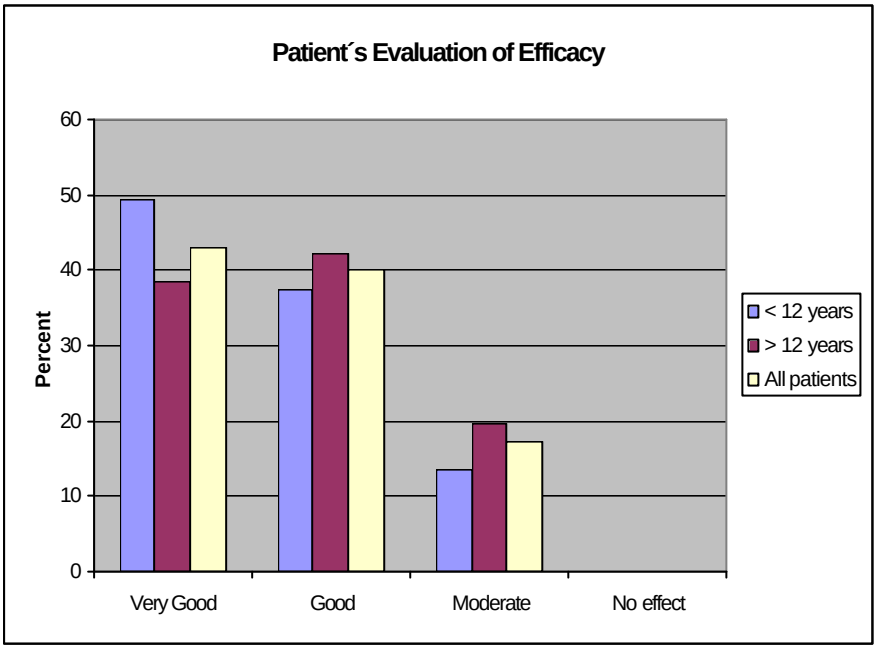
compliance with „very good“, „good“, „moderate“ or „non-compliant“. The evaluation of efficacy showed that 42.9% of the patients assessed efficacy with „very good“, 40.0% with „good“, whilst 17.1% assessed efficacy with „moderate“. No patient assessed efficacy with „no effect“. The results of the physicians' evaluation for efficacy were similarly positive as that of the patients. In 47.1% of the cases physicians assessed efficacy with „very good“, 40.0% with „good“, 11.5% with „moderate“ and 1.4% with „no effect“.

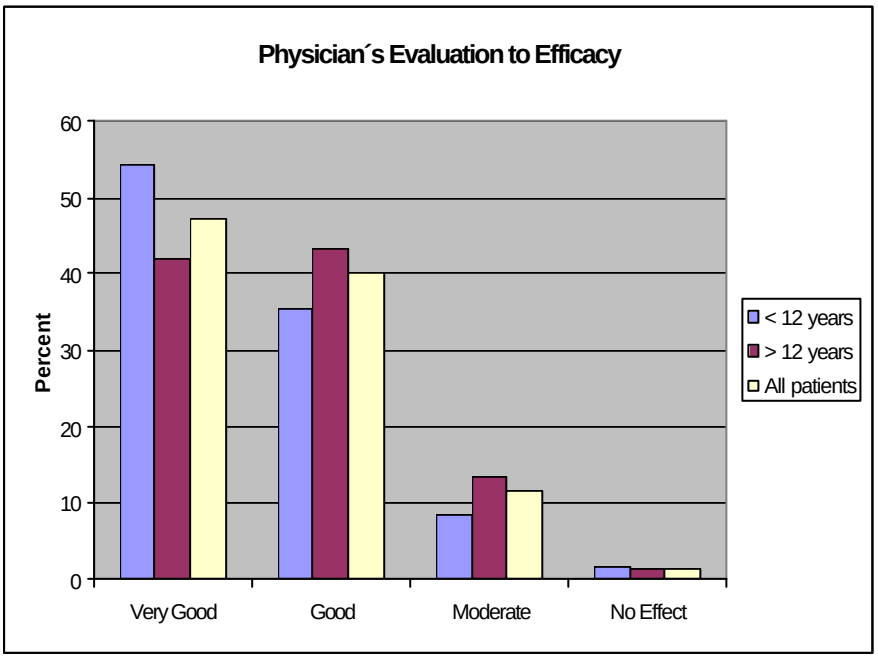
Compliance (N = 124) was assessed by the physicians to be „very good“ for 76 patients, „good“ for 38 patients and „moderate“ for 10 patients. Hence 80.3% of all patients participating in the study were given a „good“ or „very good“ compliance rating. No patient was assessed to be „non-compliant“.

5.2 Evaluation of Tolerance by Physician and Patient

At the conclusion of the study, an evaluation of tolerance was submitted by the physicians and patients, whereby an assessment of „very good“, „good“, „moderate“ and „no effect“ could be chosen. 59.9% of patients and 66.2% of physicians rated tolerance to be „very good“, whilst 37.3% of patients and 33.1% of physicians gave PEFRAKEHL a „good“ tolerance rating. 2.8% of the

Evaluation of Efficacy								
Patient Group	Patient´s evaluation (%)				Physician´s evaluation (%)			
	Very good	Good	Moderate	No effect	Very good	Good	Moderate	No effect
< 12 years	49,2	37,3	13,5	0	54,2	35,6	8,5	1,7
> 12 years	38,3	42,0	19,7	0	42,0	43,2	13,6	1,2
All patients	42,9	40,0	17,1	0	47,1	40,0	11,5	1,4





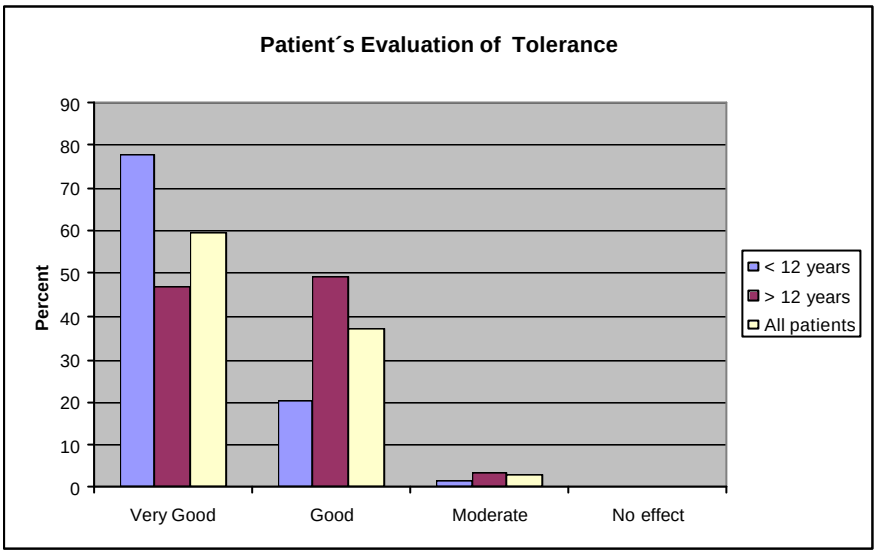
patients and 0.7% of the physicians rated with „moderate“ and neither patient nor physician with „no effect“.

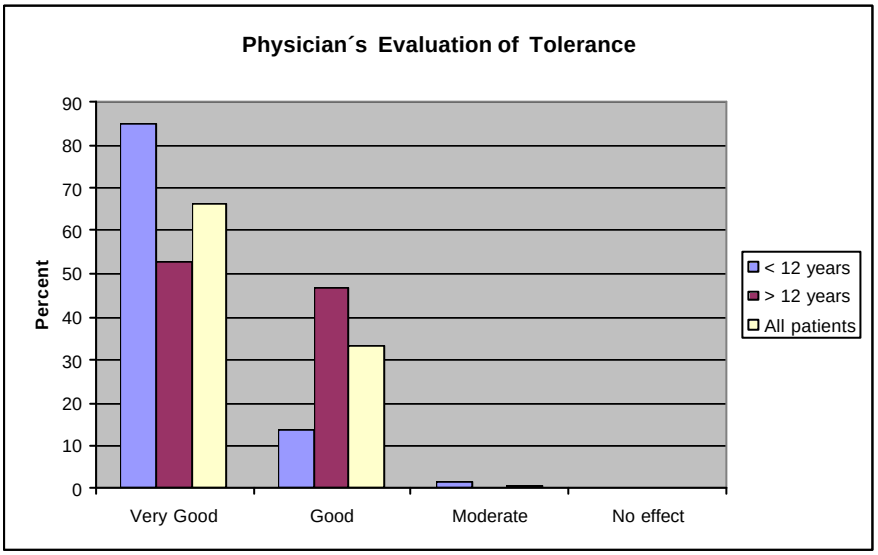
In the children group under 12 years, patients and physicians rated tolerance to be much more positive than in the adult group. Whilst in the children group 78.0% of the patients and 84.7% of the physicians rated tolerance with „very good“, this was the case in only 47.0% of the patients and 53.0% of the physicians. In the adult group no case was rated with „no effect“ by patients or physicians alike in both age groups.

5.3 Side Effects and Termination of Therapy

No therapy with PEFRAKEHL was discontinued but six cases of side effects were reported as follows: Three days after therapy begin with PEFRAKEHL drops for oral intake (1x daily 8 drops) with a 10-month old boy with intestinal mycoses, frequent crying was reported that disappeared after the dosage was reduced. Nine days after therapy begin with PEFRAKEHL drops for oral intake (1x daily 8 drops) scarlet fever was reported with a 6-year old boy. The same physician reported bronchitis in another case after six therapy days with PEFRAKEHL drops for oral intake. In both cases, a connection with the test preparation is most probably to be excluded. Four weeks after therapy begin with PEFRAKEHL ointment in a 49-year old patient, a grippal infection and an intercostal neuralgia was reported. Six weeks after treatment with PEFRAKEHL ointment in a 50-year old patient, diarrhoea and after seven weeks nasal cartarrh was stated and the same physician also reported another case of nasal catarrh after six weeks treatment with oinment in a 48-year old female patient. In no case, a connection with the PEFRAKEHL treatment could be shown.

Evaluation of Tolerance								
Patient Group	Patient´s evaluation (%)				Physician´s evaluation (%)			
	Very good	Good	Moderate	No effect	Very good	Good	Moderate	No effect
< 12 years	78,0	20,3	1,7	0	84,7	13,6	1,7	0
> 12 years	47,0	49,4	3,6	0	53,0	47,0	0	0
All patients	59,9	37,3	2,8	0	66,2	33,1	0,7	0





Side effects were reported for the different administration forms. In six cases of treatment with PEFRAKEHL injection, local irritation at the injection area was reported that disappeared without any further therapy.

Between the 3rd and the 12th therapy day, diarrhoea was reported with capsule monotherapy of intestinal mycoses (3 cases) and with combination therapy (capsules and ointment) of anal eczema (1 case). Maintaining the dosage, the complaints improved completely. The same applies to 8 cases of tenesmus. Three cases of fatigue were reported with the combination therapy of capsules and ointment (2 cases) and capsules and s.c. injection (1 case). The therapy was continued without any alterations and the complaints vanished completely during further treatment.

Between the 2nd and 20th therapy day of treatment with PEFRAKEHL capsules and s.c. injection, a 26-year old female patient with intestinal mycoses complained of dryness of the mouth. The patient was treated 77 days without any dosage alteration. After the 20th treatment day, the complaints vanished. In no case was the therapy interrupted or discontinued. In total, no difficult controllable reactions occurred. All side effects were completely reversible.

6. Summary

A total number of 142 patients in 11 medical practices (7 specialising in general medicine, 3 in internal medicine and 1 TNE specialist) participated between July 1993 and November 1999 in an application study with the preparation series PEFRAKEHL in various administration forms, such as capsules, drops, suppositories, ointment and injection.

The patients' age varied between 3 months and 80 years. Over 40% were under 12 years.

PEFRAKEHL, according to Isopathy, was mainly used in a very

wide application range, independent from the patients' age. The main indications were intestinal and skin mycoses. In the group under 12 years, in individual cases PEFRAKEHL was also applied with bronchitis, rhinitis, angina and Otitis media. Accompanying therapies were to be documented in the evaluation form.

Amongst the children (< 12 years) the therapy lasted on average 69.0 ± 110.3 days and was only 12 days shorter than in the adult group with 81.7 ± 67.7 days.

The therapeutic progress was determined by evaluations conducted at the beginning and the end of the therapy. The evaluation of efficacy showed that 82.9% of the patients and 87.1% of the physicians assessed efficacy with „very good" and „good". The evaluation of tolerance showed that 97.2% of the patients and 99.3% of the physicians rated tolerance with „very good" and „good". No therapy was discontinued and no serious side effects were reported. Side effects and intolerabilities were documented. All of them were completely reversible without any additional therapy. A possible connection with the PEFRAKEHL therapy could only be stated in six cases (irritation of the injection site).

The evaluation of tolerance and efficacy was assessed to be much better in the group under 12 years than in the adult group.

Werdorf, 8 June 2001

Dr. Reiner Heidl