



Statistical Evaluation
An Observation Study in the Application of the
Preparation Series

NIGERSAN

In the Administration Forms of: Capsules, Tablets
Drops, Suppositories, Solution for Injection

Pharmaceutical Enterprise:

Sanum-Kehlbeck GmbH & Co KG
Hoya

by Dr. Reiner Heidl
Germany



Introduction

From July 1993 to November 1999 a total of 63 patients were tested by 9 Doctors practices (5 General Practitioners, 3 Internists and 1 Ear, Nose and Throat Specialist) in an observation study with the application of the preparation series Nigersan in the following administration forms: capsules, tablets, drops, suppositories and solution for injection. The homeopathic test preparation Nigersan comprising of the 3rd to the 7th decimal dilutions of *Aspergillus niger* each according to administration dosage

- Nigersan drops contain *Aspergillus niger* D5 dil. in accordance with Prescription 5a HAB 1.
- 1 ampoule of Nigersan solution for injection contains 1 ml *Aspergillus niger* D5 (*Aspergillus niger* D6 and *Aspergillus niger* D7) aquos. dil. in accordance with Prescription 5b and 11 HAB 1.
- 1 Nigersan tablet contains 250 mg *Aspergillus niger* D5 trit. in accordance with Prescription 6 HAB 1.
- 1 Nigersan capsule contains: 330 mg *Aspergillus niger* D4 trit. in accordance with Prescription 6 HAB 1.
- 1 Nigersan suppository contains: 0.2 g *Aspergillus niger* 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 exclusive 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 had received at least one dose of the medicament.

Participating Patients

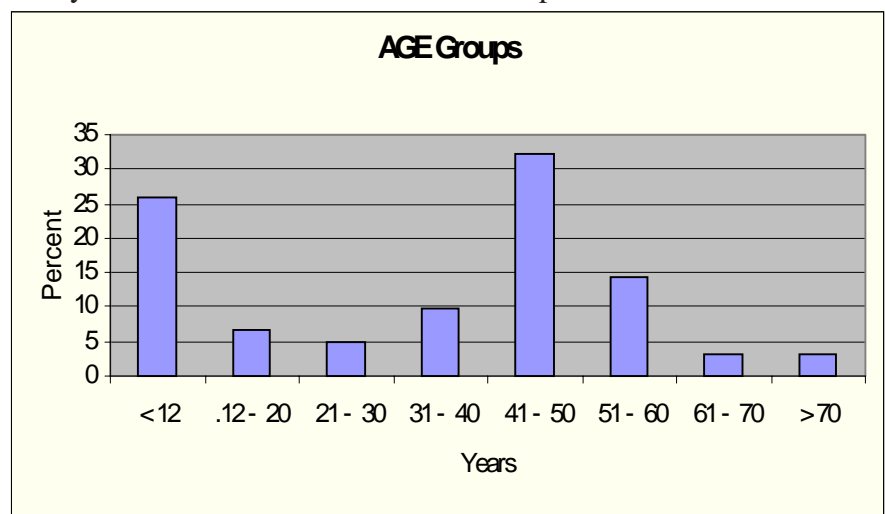
63 patients (34.9% men and 65.1% women) took part in the study. The age of the patients varied between 1 and 79 years with an average of 34.7 years and a standard deviation

of 21.0 years. A quarter of the patients (25.8%) were under 12 years of age. 6.5% of the patients were aged between 13 and 20, 4.8% of the patients were aged between 21 and 30 and between 31 and 40 made up 9.7% of the patients. Apart from the under 12 age group, the age group between 41 and 50 was the largest with 32.3% of patients. The age group between 51 and 60 was 14.5% and from 61 to

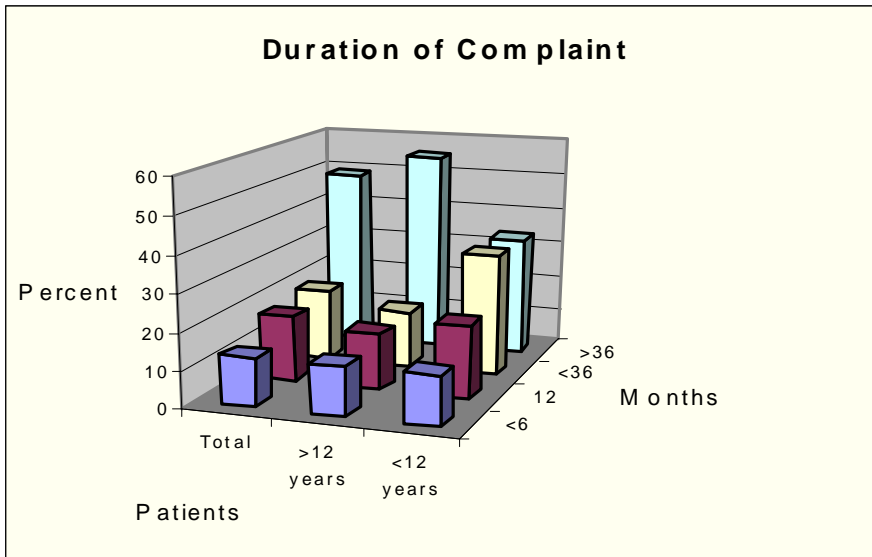
70 and over 71 years totalled 3.2% each. The age structure of the men was classified with an average age of 35.9 ± 23.2 years similar to the women with 34.0 ± 19.7 years. Height varied between 69 and 194 cm with an average of 157.1 ± 27.1 cm. Body weight lay between 9.5 and 103 kg with an average of 60.0 ± 22.4 kg.

Diagnosis and Accompanying Diseases

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



Whilst Nigersan was mainly applied in the younger patient groups under 12 years with defence weaknesses, rhinitis, bronchitis, angina and neurodermatitis, patients in the over 12 age group stood in the foreground with diseases such as hypertension, mycosis, lymphatism and bronchitis. Collected findings were carried out each before and after completion of the treatment and accompanying therapies to be



Duration of the medium term therapy in children (< 12 years) was on average 77.7 ± 82.4 days, comparable with the adult group with a medium term therapy of 63.8 ± 61.4 days. With over a third of the adult patients (=34.8%) the brief therapy of up to 25 days was predominant whilst a therapy period between 25 and 50 days with the children was the maximum expression available in 37.5% of all cases.

Dosage

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

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. Whilst doing 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 8 patients (13.3%), 11 patients (18%) between 6 and 12 months and for 12 patients (19.7%) up to 3 years. Almost half the patients (30 patients = 49.2%) suffered discomfort for over 36 months. There were no details for 2 of the patients. In the under 12 age group, almost a third of all patients suffered discomfort for between 12 to 36 months and longer than 36 months respectively, making chronic diseases stand in the foreground of the therapy with the Nigersan preparation group.

cations.

Dosage and Duration of Treatment

Time of Consultation and Duration of Treatment

Corresponding to the nature of application observation no rigid time

Duration of Complaint (Months)	Total Patient Population (%)	Patients < 12 Years (%)	Patients > 12 Years (%)
< 6	13.1	13.3	13.3
12	18.0	15.6	20.0
> 36	19.7	15.6	33.3
< 36	49.2	55.6	33.3

limit was laid down for a final examination which was carried out in a time span between 4 and 392 days with an average of 66.4 ± 67.6 days. Particularly noticeable here was a 372 day therapy of a 5 year old girl and a 392 day therapy of a 70 year old woman.

Nigersan Drops

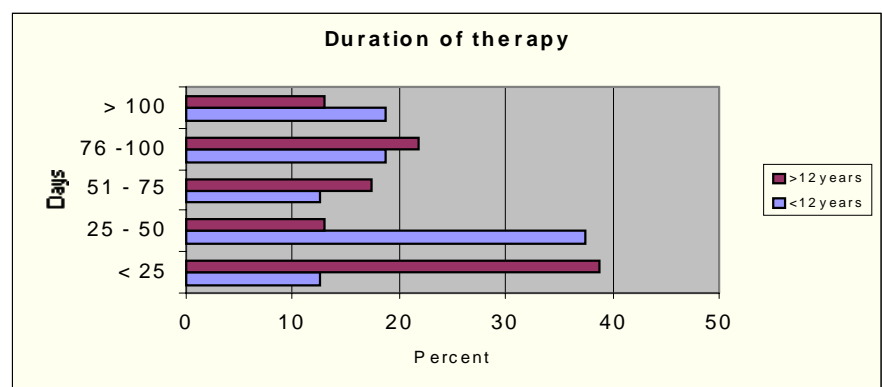
For oral intake: 1 x 8 drops daily before mealtimes

For inhalation: 2-3x daily inhale 20- 30 drops

For topical application:

a) 1 x daily 5-10 drops at the

Of the 63 patients included in the study, 10 patients (5 patients < 12 years, 5 patients > 12 years) were previously treated with Nigersan. In this connection it was arrived at that the main use of capsules and drops were tolerated without any compli-





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

Nigersan Solution for Injection

2 x weekly inject 1.0 ml either i.m., s.c., i.c., or i.v.

Nigersan Tablets

Daily 1-3 tablets to be taken with some fluid either after supper or mornings, two hours before breakfast.

Nigersan Capsules

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

Nigersan Suppositories

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

With reference to the dosage forms, 10 patients were prescribed capsules, 19 patients with tablets, 14 patients with drops for oral intake, 10 patients with drops for topical application, 9 patients with drops for inhalation, 10 patients with suppositories and 12 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.

Nothing else was substantially administered for the under and over

12 age groups. The dosage of the drops for inhalation was almost 4-fold increased with the adult groups in comparison with the children's group, however, this statement is not secure as only 3 patients in the adult groups had received drops for inhalation.

capsules, 1 patient with tablets and 1 patient with drops for oral intake. 3 of the patients were prescribed with drops for oral, topical and inhalation application. In addition to oral application with each patient, the drops were also applied topically and inhaled. Topically admin-

Total Population	Medium Dose	Minimum Dose	Maximum Dose
	%	%	%
Capsules	1.9 – 1.1	1	5
Tablets	1.4 – 0.7	1	3
Drops (oral)	7.6 – 1.3	5	10
Drops (topical)	6.5 – 2.4	2	10
Drops (inhale)	15.6 – 14.3	3	40
Suppositories	1.0	1	1
Injection (ml)	1.6 – 0.5	1	2

All Patients under 12 Years				
	Medium Dose	Minimum Dose	Maximum Dose	No. of Patients
	%	%	%	%
Drops (oral)	7.4 – 1.1	4	5	9
Drops (topical)	6.2 – 2.3	5	8	8
Drops (inhale)	8.3 – 7.2	3	24	6
Suppositories	1.0	1	1	1

All Patients over 12 Years				
	Medium Dose	Minimum Dose	Maximum Dose	No. of Patients
	%	%	%	%
Capsules	1.6 – 0.5	1	2	9
Tablets	1.4 – 0.7	1	3	19
Drops (oral)	7.8 – 1.6	5	10	5
Drops (topical)	7.5 – 2.5	5	10	2
Drops (inhale)	30.0 – 14.1	10	40	3
Suppositories	1.0	1	1	9
Injection ml	1.5 – 0.5	1	2	11

Besides the mono-therapy with one administration form, two or even three administration forms were also combined into the therapy. Because the injection was applied in weekly rotation, in addition to the injection free time 7 patients were prescribed

istered drops by each patient were further combined with tablets and capsules respectively and 1 patient combined tablets with drops for inhalation.

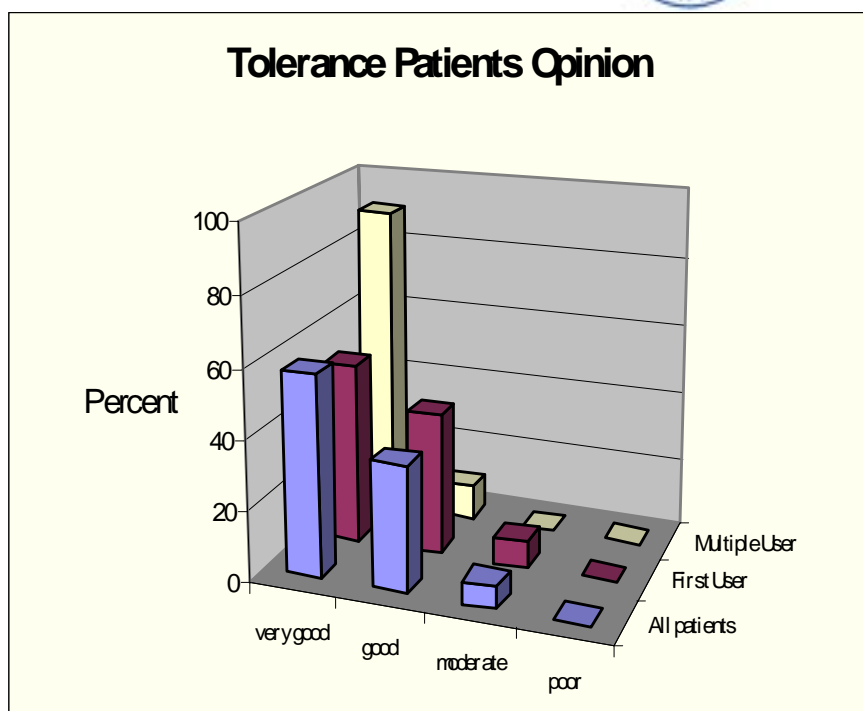
There was a clear difference in both



age groups in the extent of the combination of the dosage forms. The under 12 age group were mainly administered with drops for oral intake, topical application and for inhalation combined, whilst all other combination types were applied with the patients in the over 12 age group.

Comparison with Previous Therapy

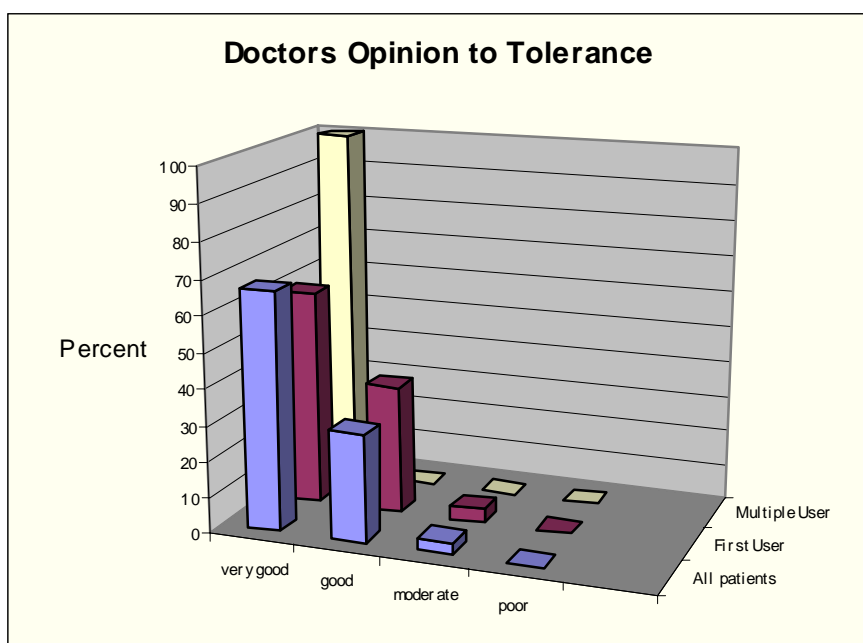
10 patients had already received therapy with one or several administration forms of Nigersan within the last five years. Although this group was very small, both the patient groups of the First and



Patient Group	Opinion to Tolerance							
	Patients Opinion				Doctors Opinion			
	Very Good %	Good %	Moderate %	Poor %	Very Good %	Good %	Moderate %	Poor %
All patients	57.8	35.9	6.3	0	66.7	30.2	3.2	0
First User	51.9	40.7	7.4	0	60.4	35.8	3.8	0
Multiple User	90.0	10.0	0	0	100.0	0	0	0

Multiple Users were compared with respect to effectiveness and tolerance. From the data on tolerance, the possibility of tendencies towards sensitisation from the pharmaceutical effective components should be possible.

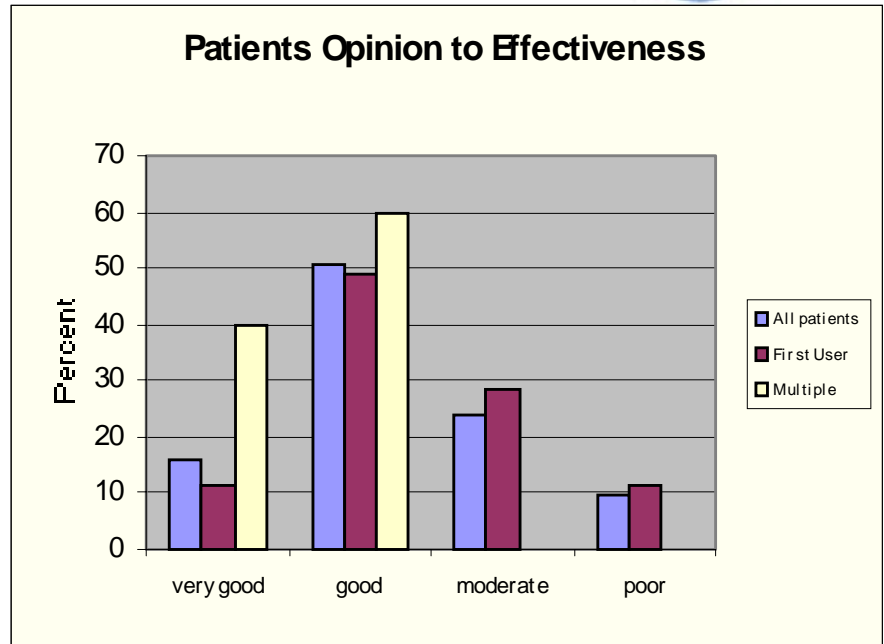
Opinion to tolerance by multiple application was substantially better than that of a single application. Patients in the Multiple Users group gave an overall assessment of "very good" and "good" and 100% of the doctors gave an assessment of "very good". The designation of "very good" tolerance was



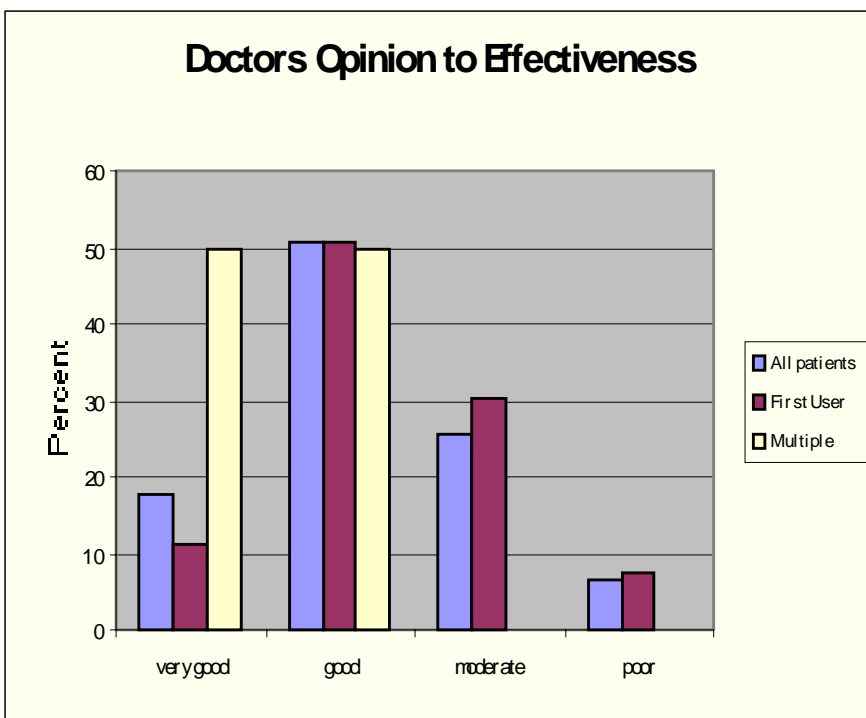


substantially more pronounced in this group than with the total average. From this data, it is shown that there was no potential of an exposure to danger regarding sensitisation to patients through the pharmaceutical effective component of *Aspergillus niger*.

The Multiple Users judged the effectiveness in keeping with the trend better in the assessment "very good" than the First Users, just as no multiple user gave an assessment of "moderate" and "no effect". The duration of the therapy is also distinguished by the Multiple Users



Patient Group	Opinion to Effectiveness							
	Patients Opinion				Doctors Opinion			
	Very Good %	Good %	Moderate %	Poor %	Very Good %	Good %	Moderate %	Poor %
All patients	15.9	50.8	23.8	9.5	17.5	50.8	25.4	6.3
First User	11.3	49.1	28.3	11.3	11.3	50.9	30.2	7.5
Multiple User	40.0	60.0	0	0	50.0	50.0	0	0

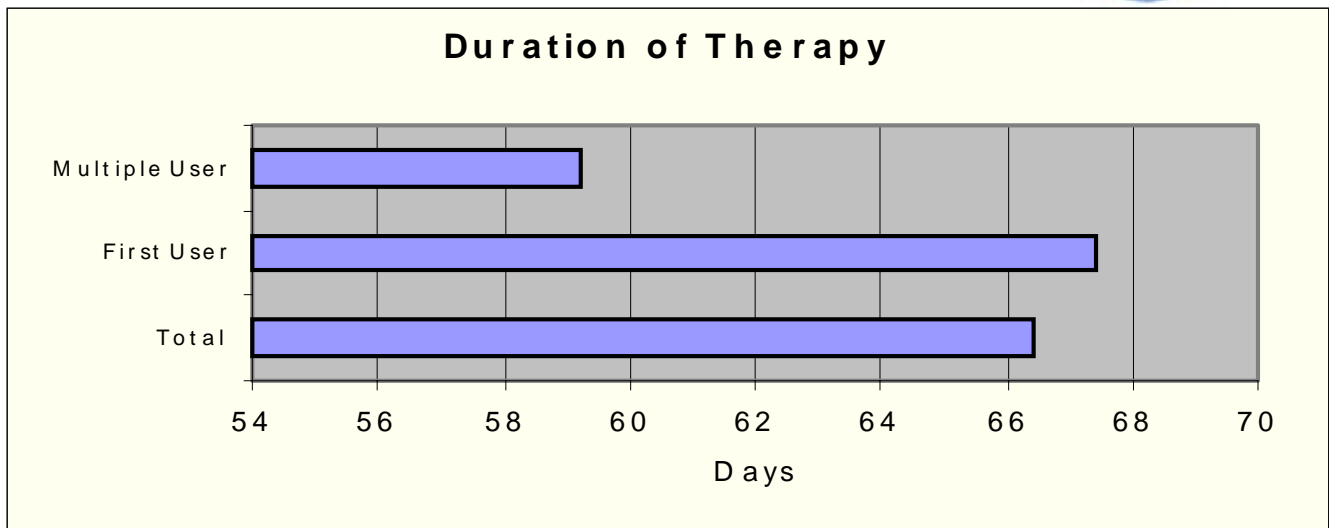


with an average therapy duration of 59.2 ± 30.9 days, a reduction of 14% compared with the average. The First Users were treated for an average of 67.4 ± 72.6 days.

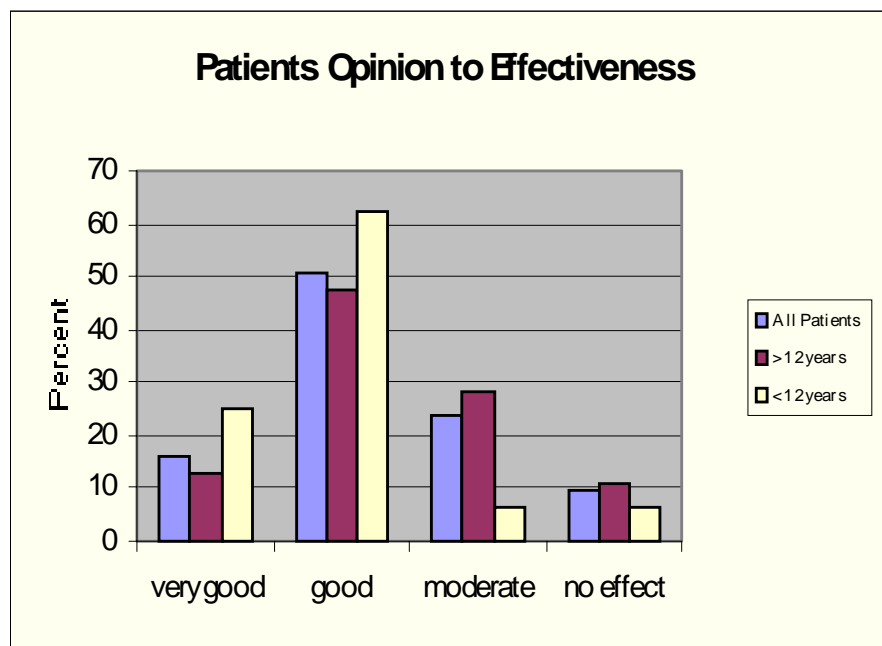
Effectiveness and Tolerance

Assessment of Effectiveness by Doctor and Patient

In a closing assessment, doctors and patients were asked to judge the effectiveness and tolerance. The effectiveness could be assessed with "very good" "good" "moderate" or "no effect". In addition the doctors

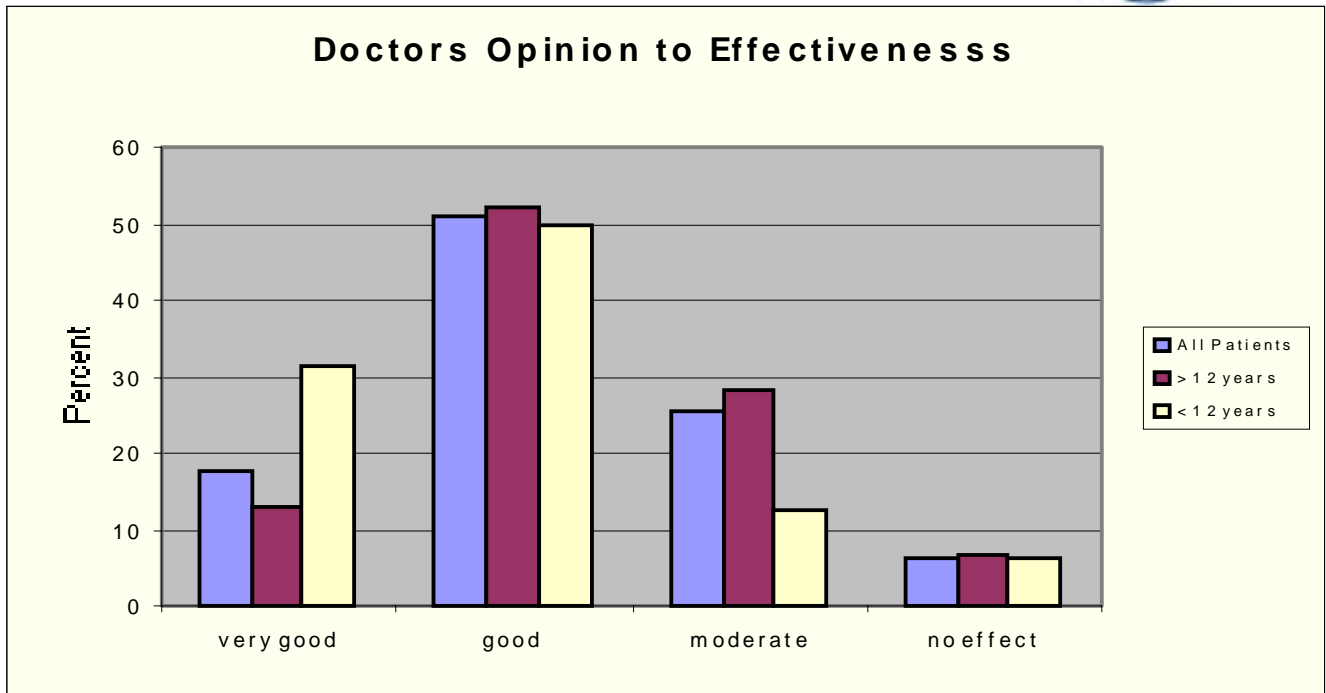


were asked according to the patient's compliance to usage, so that it could also be classified with "very good", "good", "moderate" or "poor". 15.9% of patients expressed effectiveness with "very good", 50.8% with "good" whilst 23.8% expressed only "moderate" and 9.5% with "no effect". The doctors assessment to effectiveness was just as positive as with the patients. 17.5% of patients were classified with "very good", 50.8% with "good", 25.4% with "moderate" and 6.3% with "no effect".



Application behaviour (N=58) was judged by 34 patients with "very good", "good" by 21 patients and "moderate" for 3 patients as reported through their doctor. With

Patient Group	Opinion to Effectiveness							
	Patients Opinion				Doctors Opinion			
	Very Good %	Good %	Moderate %	No Effect %	Very Good %	Good %	Moderate %	No Effect %
All patients	15.9	50.8	23.8	9.5	17.5	50.8	25.4	6.3
< 12 Years	13.0	47.8	28.3	10.9	13.0	52.2	28.3	6.5
> 12 Years	25.0	62.5	6.3	6.3	31.3	50.0	12.5	6.3

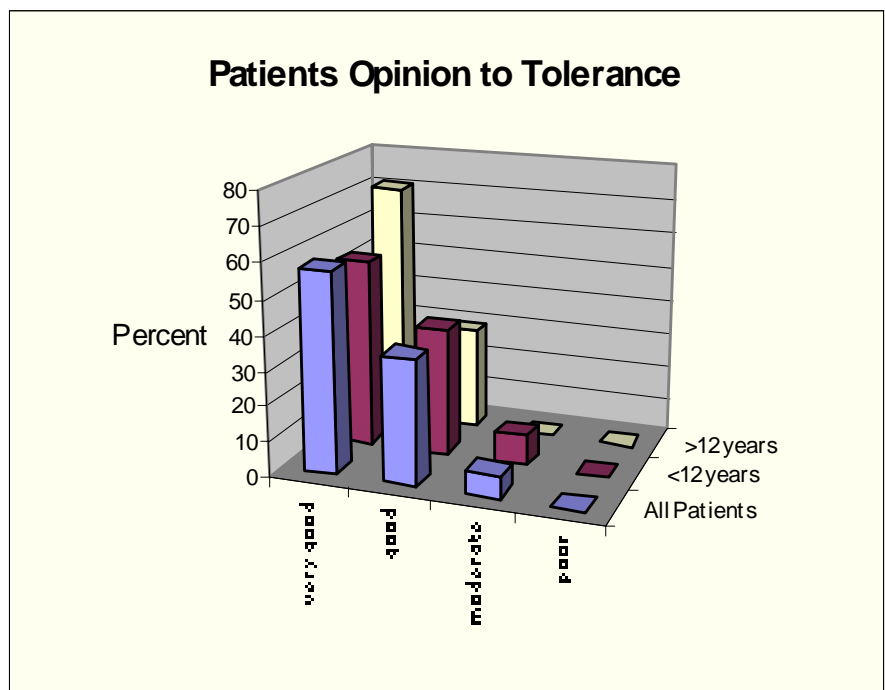


it 94.8% of all those patients involved in the study confirmed "very good" and "good" compliance. This was only "moderate" for two patients and "poor" for none of the patients.

Opinion of Tolerance by Doctor and Patient

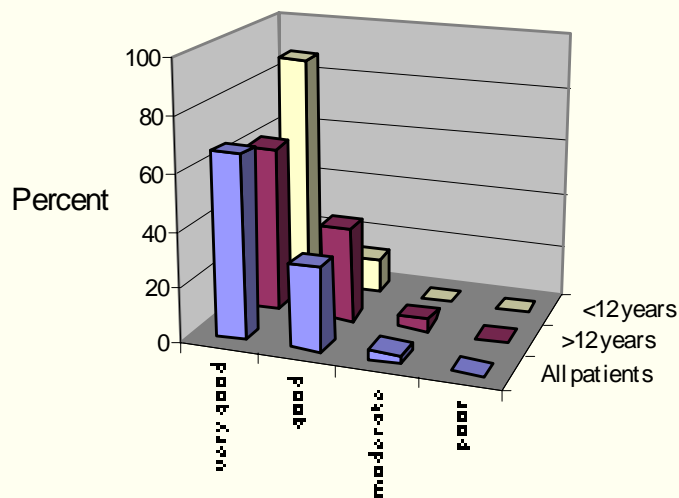
To conclude the examination, an assessment to tolerance was submitted from doctors and patients whereby a judgement of "very good", "good", "moderate" and "poor" could be chosen. 57.8% of patients and 66.7% of doctors classified the tolerance with "very good" whilst 35.9% of patients and 30.1% of doctors confirmed a "good" tolerance with Nigersan. A "moderate" tolerance was given by 6.3% of patients and 3.2% of doctors. No patient or doctor gave a classification of "poor".

Tolerance was by far more positively assessed by doctors and pa-



Patient Group	Opinion to Tolerance							
	Patients Opinion				Doctors Opinion			
	Very Good %	Good %	Moderate %	Poor %	Very Good %	Good %	Moderate %	Poor %
All patients	57.8	35.9	6.3	0	66.7	30.1	3.2	0
< 12 Years	54.3	37.0	8.7	0	60.9	34.8	4.3	0
> 12 Years	70.6	29.4	0	0	87.5	12.5	0	0

Doctors Opinion to Tolerance



tients in the under 12 age group than with the over 12 age group. No assessments of "moderate" or "poor" were given, but only "very good" and "good". 70.6% of patients and 87.5% of doctors in the younger age groups indicated tolerance as "very good" and by the over 12 age groups this assessment was indicated by only 54.3% of patients and 60.9% of the doctors.

Side Effects and Discontinuation of the Therapy

The therapy with Nigersan was not discontinued by any of the patients. However 8 cases of side effects were reported and are more closely interpreted as follows: A 48 year old female patient complained of tiredness and sweating between the 6th and 11th day of treatment with capsules., however these symptoms disappeared again without any further therapy. A connection with the Nigersan therapy was ruled out as

this patient was also receiving therapy for a gynecological indication. Two patients aged 48 and 50 with Morbus Bechterew disease both showed irritation at the point of needle insertion (i.m.) between the 4th and 21st and 35th day of treatment respectively which, however, both improved without any further measures being taken. Between the 3rd to 8th and 10th treatment days respectively, both patients complained of an increased stiffness of the joints and pain. These must be classified as a primary deterioration.

A 44 year old female patient had irritation at the point of injection between the 3rd and 11th day of treatment which disappeared again without any additional measures being taken. One hour after an i.v. injection, a 50 year old male patient experienced sweating lasting for two to three days which disappeared again without any further therapy. The day after the injection this

patient also complained of prolonged fatigue over a five day period. After daily administration of two Nigersan capsules a 28 year old female patient complained of a general weakness between the 3rd and 11th day of treatment which afterwards disappeared. The doctor indicated a connection with the Nigersan therapy as improbable. Circa two minutes after the insertion of a suppository, a 79 year old male patient always complained of perianal itching and heat sensation for a duration of 10 minutes after which no further discomfort was experienced. Side effects were reported in 4 cases. Fever was reported with a 7 year old girl who received therapy for chronic rhinitis. With two girls aged 4 and 5 a chicken pox infection was reported which was then further treated by conventional means. A side effect of recurring infection was reported with 1½ year old boy who received therapy for a recurring influenza infection and sleep disturbances. The suitability of this information must be questioned. After assessment of all data, side effects are to be reduced to reactions at the point of needle insertion by injections. All other data bear no relation either to the suitability or are not to be brought into connection with the Nigersan therapy.

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

Summary

From July 1993 to November 1999 a total of 63 patients were tested



by 9 Doctors practices (5 General Practitioners, 3 Internists and 1 Ear, Nose and Throat Specialist) in an observation study with the application of the preparation series Nigersan in the following administration forms: capsules, tablets, drops, suppositories and solution for injection.

The age of the patients varied between 1 year and 79 years. Almost a quarter of the patients were under 12 years of age. Nigersan 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 group under 12 years, Nigersan was mainly applied with defence weaknesses, rhinitis, bronchitis, angina and neurodermatitis. In the over 12 age group diseases such as hypertonia, mycosis, lymphatism

and bronchitis were predominant. Accompanying therapies were to be documented in the survey form.

The duration of the medium term therapy for children (<12 years) was on average 77.7 ± 82.4 days, comparable with the adult group medium term therapy with 63.8 ± 61.4 days.

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

Approximately two thirds of the patients and doctors (66.7% and 68.3%) described the effects of the treatment as "very good" and "good". Tolerance was judged by 93.7% of the patients and 96.8% of doctors each with "very good" and "good". There was no break in the study. No serious side effects were observed. Side effects and intolerance were documented.

These were mostly all without additional therapy and completely reversible. A connection with the Nigersan therapy could only be made up in only 3 of the cases where irritation at the point of needle insertion occurred. Tolerance and effectiveness in the under 12 age group was substantially more positively judged as with the over 12 age group.

Werdorf, 19. February 2001

Dr. Reiner Heidl

© Copyright by Semmelweis-Institut GmbH 27318 Hoya, Germany

All Rights Reserved