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# IgG-mediated food allergy as trigger of fibromyalgia complaints and the influence of an elimination diet

Dissertation
for acquisition of a Doctoral Degree in Medicine at the Medical Faculty of
Ludwig Maximilian University in Munich

Submitted by Mario Krause
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2005

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Date of oral examination: October 6, 2005

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# 1. Introduction

Functional and psychovegetative complaints of fibromyalgia patients (e.g. polytopic pain, stress intolerance, lassitude, migraines, depressions, sleep disorders, rapid fatigability, etc.) and especially irritable colon are similar to the complaints of patients with food allergies or food intolerances. Specific histological changes are absent up to now; cellular inflammatory signs cannot be detected. A deterioration of symptoms is frequently found with intermittent inflammatory illnesses. Spontaneous remissions are described, but this frequently concerns a chronic clinical picture. Physiotherapy procedures, heat applications, antidepressants, NSAID or corticoids will normally be employed for therapy.

The motive for initiation of this project was unsolicited feedback from fibromyalgia patients who reported a clear improvement of their symptoms due to a dietary change and studies which showed a positive influence of a dietary change in patients with rheumatoid arthritis [15,25,27,43,48]. The investigator was motivated through research regarding chronic fatigue syndrome (CFS) and food intolerances [9,33,54] and the works from Enestrom, who was able to prove an augmented IgG deposition in the skin of fibromyalgia patients [19,20].

The greatest challenge in the handling of food allergies and food intolerances is the identification of the responsible foodstuff. The differentiation of allergic reactions and intolerances is difficult. A clarification with RAST and prick test is generally insufficient [7,21,23,34,47,50]. The aim was to find new therapeutic approaches in the treatment of fibromyalgia through differentiated investigative.

## 1.1. Definitions

The term “food intolerance” is not to be equated with any specific reaction and first of all signifies merely a reproducible adverse reaction to a special foodstuff or a substance contained in this foodstuff. Immunological reactions (in the narrow sense, food allergy), enzymatic defects, pharmacological reactions, irritations and toxic effects come into question as mechanisms of a food intolerance. The term “food allergy” is frequently misused and thus does not take the causes into consideration [6,17,36,46].

### 1.1.1. Food allergy

An allergic reaction is a reproducible adverse reaction to a substance which is mediated through an immunological process. This can be mediated through antibodies, mast cells or circulatory immune complexes. A food allergy is accordingly such a response to foodstuff. The “American Academy of Allergy and Immunology Committee on Adverse Reactions of Food” defines a food allergy as “an immunological reaction which is attributable to the intake of food or additives” [6]. Food allergies can be found via all types, according to Coombs, from I to IV or in any combination. The term “food allergy” is traditionally equated with type I, whereas types II, III and IV are designated as immune-mediated intolerances. The IgG-mediated problem investigated here thus concerns an allergy predominantly ascribed to type III or an immune-mediated intolerance. The processes proceeding within the framework of the allergy occur via predominantly inflammatory paths. At the same time, the triggering allergenic substance can be ingested, injected, inhaled or otherwise come into contact with skin or mucosa.

The reaction occurs on a delayed basis within 8 to 72 hours after ingestion. Therefore an affected individual can only react with gastrointestinal problems on Friday to a foodstuff which he/she had already consumed on Wednesday. This is why, long-term, this form of food allergy is frequently neither recognized by the affected individuals nor the attending physicians.

### 1.1.2. Anaphylaxis or anaphylactic shock

In this case this concerns a life-threatening, rapid allergic reaction with circulatory collapse. The term “anaphylaxis” is still erroneously equated with allergic reactions which are mediated through IgE antibodies. At the same time, the milder forms of an IgE-mediated allergy such as pollenosis are erroneously equated with this severe reaction.

### 1.1.3. Food intolerance

The intolerance does not presuppose any specific type or mechanism, and is defined as a reproducible adverse reaction to a specific foodstuff or an ingredient.

### 1.1.4. Enzymatic food intolerance

Congenital or acquired metabolic defects on account of enzyme defects can interfere with the digestion and absorption of carbohydrates, proteins or fats. One example is

lactose intolerance through lactase deficiency in the intestinal mucosa.

### 1.1.5. Pharmacological food intolerance

Pharmacological substances in food can also trigger adverse reactions. Coffee is able to cause intestinal and cardiac side effects, whereas sodium nitrate can cause vascular dilatation with flush, headache and urticaria [8]. Vasoactive amines (tyramine, serotonin, tryptamine, histamine and others) are contained in various foodstuffs as normal ingredients, e.g. tuna fish, sardines, bananas, cheese, yeast extract, chocolate, wine, spinach and tomatoes. Side effects can appear through high supply, bacteriological interactions, interactions with pharmaceuticals (MAO inhibitors), release from mast cells and other inflammatory mediators. The symptoms vary from flush, constriction of the smooth musculature of the intestine and the bronchia, tachycardia, headache, changes in blood pressure, etc.

### 1.1.6. Mucosal irritations

Some foodstuffs have a directly irritating effect on the mucosa of the mouth or intestine, such as coffee, curry or hot spices.

### 1.1.7. Toxic food intolerances

Many plants contain toxins in order to protect themselves against their predators, such as solanine in potatoes, cyanides in tapioca, mycotoxins in fungi and cereals, phototoxic furocoumarins in angelica, parsley and dill. The toxic reactions are manifold.

### 1.1.8. Food aversion

An aversion to certain foodstuffs on account of psychological reasons (e.g. bad taste, the desire to lose weight) is to be distinguished from allergies and intolerances.

### 1.1.9. Psychological intolerance

Here this concerns a physical reaction which is triggered through emotions, less through the foodstuff itself. The emotions can have a direct connection to the ingested foodstuff or also be independent of this.

### 1.1.10. Strain on the organism through food

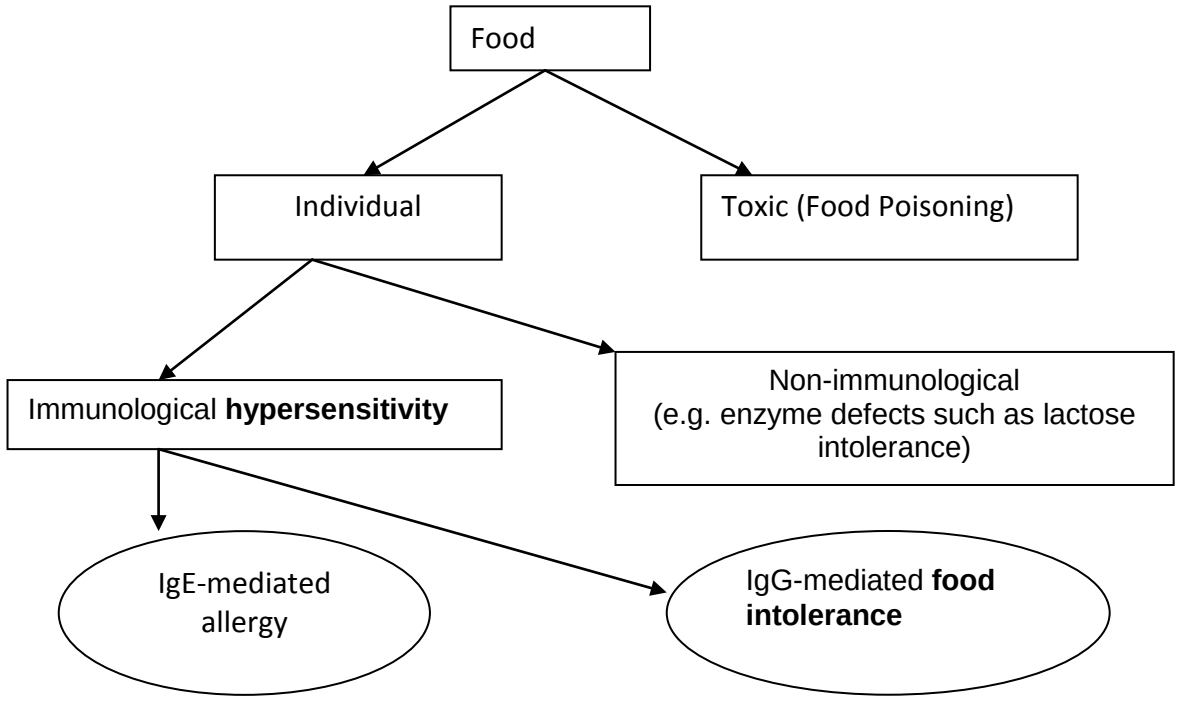



Figure 1

## 1.2. Clinical symptoms of a food allergy

Urticaria, angioedemas, rhinitis, atopic reactions, asthma, nausea, abdominal symptoms (pain, diarrhea, constipation, increased bowel activity, hemorrhoids, bloody stool), rheumatoid complaints, myalgias, migraines, etc.

### 1.2.1. Sequence of allergic reactions

Most allergic reactions to foodstuffs occur within a few minutes after ingestion. Some occur on a quite delayed basis. Hill et al. were able to differentiate three types of reactions with cow's milk allergy. The reaction times varied between 45 minutes and more than 20 hours [30].

## 1.3. Food quantity and allergic reaction

The quantity of allergen as trigger of a reaction varies. For instance, very sensitive people already react to 1 µg casein, others only with quantities greater than 200 g [30]. A connection between the ingested quantity and the period up until appearance of symptoms is also described, whereby the test persons which required greater quantities of allergen for reaction was also greater than the period up until appearance of complaints [30].

Other factors for allergic reactions:
Allergens can require other cofactors in order to bring about complaints, e.g. physical training [16,17] or medicaments (aspirin). Conversely, the tolerability can be better in a different environment or climate.

## 1.4. Frequency

Oberritter (1991) indicates the frequency of allergic illnesses for the Federal Republic of Germany (FRG) with 10-20% [46]. The British Allergy Foundation estimates the number of food intolerances in Europe and the USA at 45%. Other sources act on the assumption of 2-8% in the western world [22]. The types of allergies and food intolerances described by me thereby mix, so that no precise details can be made with regard to the frequency for the type III allergies with increased IgG levels described by me. In his paper published in 2004, Accomando points out that the proportion of non-recognized food intolerances in the example of celiac disease worldwide is very high and distinguishes classic, sub-clinical, silent and potential courses [1].

## 1.5. The importance of the elimination diet

In the treatment of food intolerances and particularly of food allergies, the question is posed as to whether it will ever be possible at any other point in time for the people to ingest the incompatible substance without reactions. A large number of children with intolerances appearing in the first year of life lost their intolerances over the course of time [8,50]. Whereas it is generally assumed that intolerances persist on a lifelong basis in adults, in a follow-up study it could be shown that one third of the adults had lost an allergy after a year-long elimination diet [48]. Fasting also represents one form of the elimination diet.

## 1.6. Pathomechanism of a type III food allergy

The special feature of the specific defense system (= acquired immunity: lifelong learning) consists in the fact that the antibodies constitute a structure, in which case it can only detect a very specific antigen ("key-lock principle"). So our immune system is able to form several thousand different antibodies which are all different in their structure and can each bind to a very specific antigen.

If an antigen infiltrates into the organism, the suitable antibody adheres to it. In this way the antigen is visible for all other cells of the immune system. Bonds between antigens and antibodies are described as an immune complex. Cells which detect these immune complexes release messenger substances (mediators) and attract other immune cells. An automatically proceeding cascade of reactions develops. The immune complex is ultimately destroyed by phagocytes (scavenger cells) at the end of the reaction.

This automatism also proceeds with a food intolerance. However, here the antibody adheres to a specific foodstuff on account of the corresponding structure. But as long as incompatible foodstuffs will be consumed, this automatism is unstoppable. The immunological reaction inevitably proceeds, even if the effects can be detrimental to the body. This is clear with autoimmune diseases. Here a malfunction of the immune system leads to formation of IgG antibodies against endogenous tissue. Endogenous tissue becomes an antigen, the immune complex "endogenous tissue antibody" is "combated" through the body's own immune system. Severe illnesses can be the result.

## Goal of the paper

**The following questions shall be clarified with the paper at hand:**

1. Are IgG-mediated food allergies causally involved in the fibromyalgia syndrome?
2. Can complaints with fibromyalgia syndrome change through a dietary change?
3. Which complaints particularly improve under an elimination diet?
4. How large is the compliance with regard to the practical implementation of an immunologically optimized dietary change?
5. Does an elimination diet have an influence on body weight?
6. How do the patients themselves assess this therapy?

## 2. Patient collective and research method

In collaboration with self-help groups, men and women were sought who are afflicted with the fibromyalgia syndrome and were willing to document their experiences within the framework of such a dietary change with the help of a detailed questionnaire. The diagnosis “fibromyalgia” had to be made by a physician at least once in the anamnesis. The questionnaire encompassed 5 documentation points (start of treatment, controls after 2, 4, 6 and 8 weeks). Amongst other things, questions regarding severity of 50 specific symptoms, weight as well as dietary change (consequence, problems) were to be answered for each point in time.

The expressivity of the 50 predetermined symptoms should be assessed at all documentation points with the help of a 4-step scale ranging from 0=nonexistent via 1=less, 2=moderate to 3=severe.

Specific antibodies against 272 different substances found in foodstuffs were identified on a semi-quantitative basis and quantified in 4 classes with the help of a standardized sandwich ELISA method. Varieties of meat, fish products, yeasts and baking additives, fruit varieties, nuts and seeds, vegetable varieties, salad varieties, fungi, milk products, food additives, grain and carbohydrate-rich products, coffee and tea varieties, saccharated products, spices, eggs and also heavy metals (in terms of secondary findings) were examined in this connection.

The results of the ELISA test were discussed with the patients. The patients additionally received a detailed written interpretation of findings and a personal recipe book in which concrete cooking recipes for the ordinary routine were provided to them. The proposed cooking recipes contained only substances no specific IgG had been detected in the ELISA test.

All patients had the possibility to take advantage of unlimited nutritional advice per telephone throughout the entire examination period. The nutritional advice was strictly oriented towards the laboratory results.

In order to attain the cooperation of patients and as consistent dietary change as possible, importance was attached to an interpretation of findings understandable for the patients and concrete instructions for the implementation, and a standardized interpretation of findings with written nutritional recommendation based on this, including cooking recipes, was employed.

A total of 73 participants documented their complaints over the indicated period. The diagnosis ‘fibromyalgia syndrome’ was not checked off with 5 patients. Here this possibly concerned family members of fibromyalgia patients, in which the diagnosis is not confirmed. At any rate, these 5 patients were excluded from the evaluation, so that 68 patients ultimately form the basis of the evaluation at hand.

This patient group consisted of 60 women and 8 men aged between 20 and 69 years (mean value: 53 years). The mean body mass index (BMI) at the start of treatment amounted to 28.4 $kg/m^2$, and more than two thirds of all patients were overweight (41.2%) or obese (29.4%).

On average, the patients suffered for nearly 10 years from fibromyalgia syndrome (minimum: 1 year; maximum: 30 years).

## 2.1. Sex

Of the total 68 documented patients, 60 (88.2%) were female and 8 (11.8%) were male.

**Sex of patients**

| Sex | Number | % |
|---|---|---|
| Male | 8 | 11.8 % |
| Female | 60 | 88.2 % |
| Total | 68 | 100 % |

Table 1

## 2.2. Age

The average age of the patients recorded at the start of treatment amounted to 53.1 (± 8.8) years. The youngest female patient was 20 years, the oldest 69 years old.

**Age of patients**

| Sex | Mean Value | Standard Deviation | Minimum | Maximum | Valid |
|---|---|---|---|---|---|
| Male | 48.5 | 6.6 | 35.0 | 55.0 | N=8 |
| Female | 53.7 | 8.9 | 20.0 | 69.0 | N=6 |
| Total | 53.1 | 8.8 | 20.0 | 69.0 | N=6 |

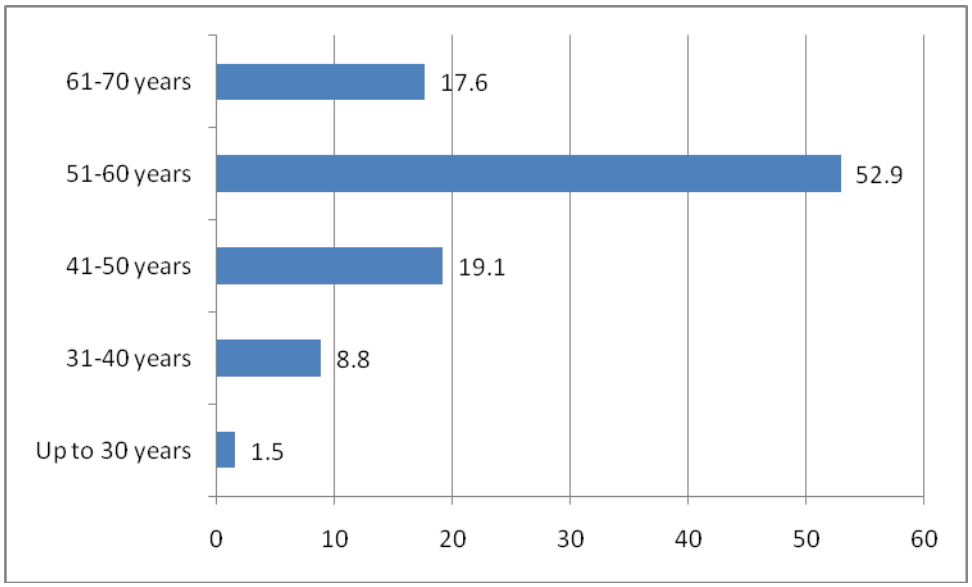
Table 2

**Age of patients (categorical)**

| | Sex | | | | Total | |
|---|---|---|---|---|---|---|
| | Male | | Female | | | |
| Age (years) | Number | % | Number | % | Number | % |
| Up to 30 years | 0 | 0 % | 1 | 1.7 % | 1 | 1.5 % |
| 31-40 years | 1 | 12.5 % | 5 | 8.3 % | 6 | 8.8 % |
| 41-50 years | 4 | 50.0 % | 9 | 15.0 % | 3 | 19.1 % |
| 51-60 years | 3 | 37.5 % | 33 | 55.0 % | 36 | 52.9 % |
| 61-70 years | 0 | 0 % | 12 | 20.0 % | 12 | 17.6 % |
| **Total** | **8** | **100.0 %** | **60** | **100.0 %** | **68** | **100.0 %** |

Table 3

**Age distribution of patient collective**




Graphic 1

## 2.3. Height, weight and BMI during admission visit

The mean body mass index at the start of treatment amounted to 28.4 kg/m$^2$ (median: 28.0 kg/m$^2$)

**Height according to sex**

| Sex | Height [cm] Mean Value | Standard Deviation | Minimum | Maximum | Valid N |
|---|---|---|---|---|---|
| Male | 178.0 | 11.8 | 166.0 | 198.0 | N=7 |
| Female | 165.2 | 6.8 | 145.0 | 182.0 | N=59 |
| Total | 166.6 | 8.4 | 145.0 | 198.0 | N=66 |

Table 4

**Weight according to sex**

| Sex | Weight [cm] Mean Value | Standard Deviation | Minimum | Maximum | Valid N |
|---|---|---|---|---|---|
| Male | 84.1 | 21.8 | 62.0 | 124.0 | N=8 |
| Female | 77.7 | 16.1 | 51.0 | 115.0 | N=60 |
| Total | 78.5 | 16.8 | 51.0 | 124.0 | N=68 |

Table 5

**Body Mass Index according to sex**

| Sex | Body Mass Index [kg/m$^2$] Mean Value | Standard Deviation | Minimum | Maximum | Valid N |
|---|---|---|---|---|---|
| Male | 27.3 | 4.4 | 22.1 | 35.1 | N=7 |
| Female | 28.5 | 5.7 | 19.2 | 45.2 | N=59 |
| Total | 28.4 | 5.6 | 19.2 | 45.2 | N=66 |

Table 6

## 2.4. Classification of initial weight

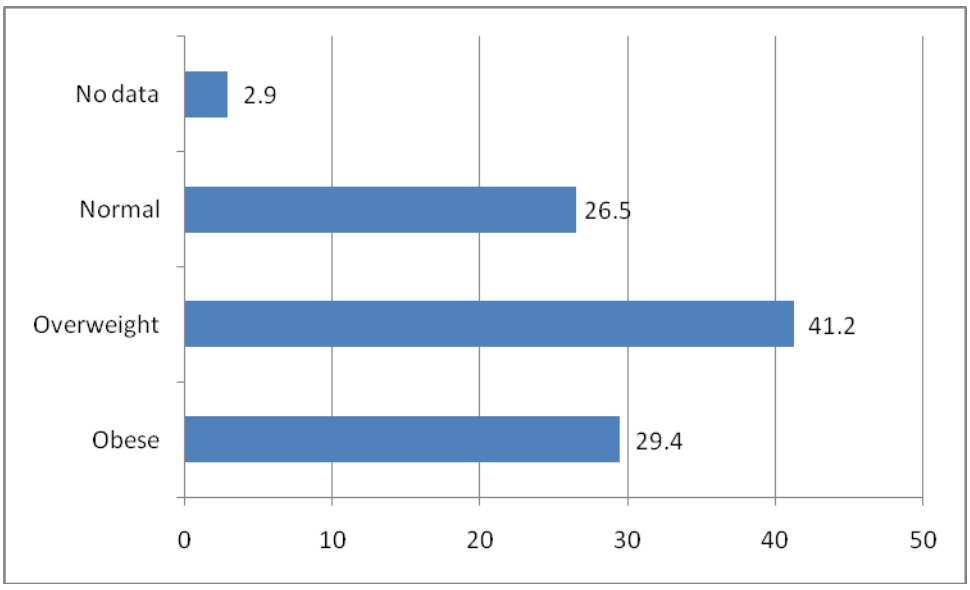
The initial examination revealed the following picture for the established BMI values: Most patients were overweight (41.2%), whereas 29.4% were obese and 26.5% of normal weight. The height data was missing with 2 patients, and so the body mass index could not be calculated.

**Classification of initial weight**

| | Sex | | | | Total | |
|---|---|---|---|---|---|---|
| | Male | | Female | | | |
| **Age (years)** | **Number** | **%** | **Number** | **%** | **Number** | **%** |
| Normal | 20 | 25.00 % | 16 | 26.7 % | 18 | 26.5 % |
| Overweight | 4 | 50.0 % | 24 | 40.0 % | 28 | 41.2 % |
| Obese | 1 | 12.5 % | 19 | 31.7 % | 20 | 29.4 % |
| No data | 1 | 12.5 % | 1 | 1.7 % | 2 | 2.9 % |
| **Total** | **8** | **100.0 %** | **60** | **100.0 %** | **68** | **100.0 %** |

Table 7

**Based on the details regarding weight and height, the BMI was established and the patients were accordingly classified according to the recommended WHO threshold values for overweight and obesity.**




Graphic 2

## 2.5. Diagnosis

All patients had indicated the diagnosis ‘fibromyalgia syndrome’. On average, the patients suffered for nearly 10 years from the illness (minimum: 1 year; maximum: 30 years; 7 patients without data). The diagnosis had been made by a physician at least once in the anamnesis.

**Fibromyalgia syndrome – when did it appear?**

| Sex | Fibromyalgia since ... [years] Mean Value | Standard Deviation | Minimum | Maximum | Valid N |
|---|---|---|---|---|---|
| Male | 6.8 | 4.4 | 3.0 | 15.0 | N=6 |
| Female | 10.0 | 7.0 | 1.0 | 30.0 | N=55 |
| Total | 9.7 | 6.8 | 1.0 | 30.0 | N=61 |

Table 8

## 2.6. General risk factors

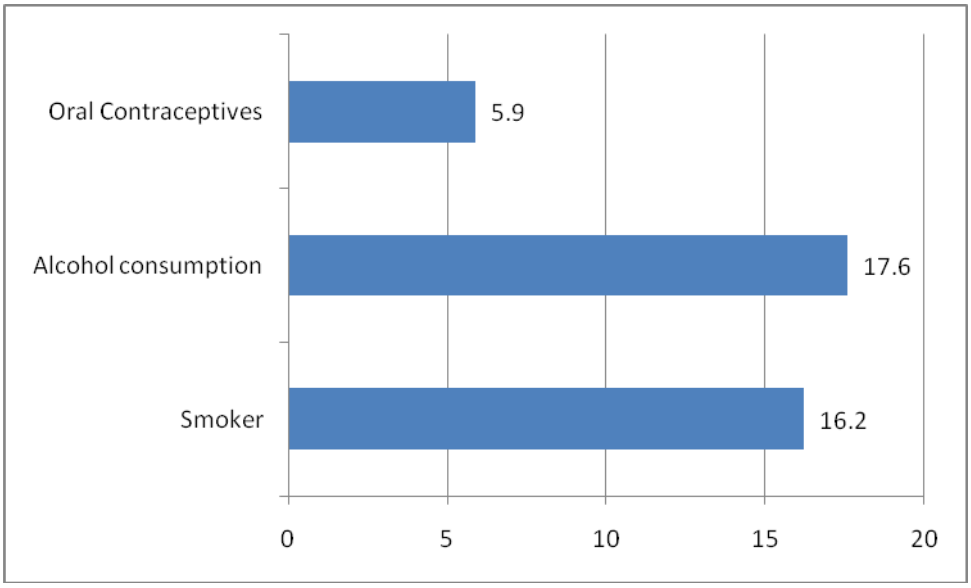
**Risk factors**

| Sex | Number | % |
|---|---|---|
| Smoker | 11 | 16.2 % |
| Alcohol consumption | 12 | 17.6 % |
| Oral contraceptives | 4 | 5.9 % |

Table 9

Percentages related to all patients – multiple mentions possible

Risk Factors




Graphic 3

# 3. Results

## 3.1. Symptoms at start of treatment

The blood test for detection of type III food allergies revealed the following results: on average, the patients had 47 food reactions, 9 of them very severe (severity 3 and 4).

The expressivities of the 50 predetermined symptoms have been documented with the help of a 4-step scale (from 0=nonexistent to 3=severe).

The expressivity of 50 predetermined symptoms at the time of the start of treatment has been processed in the following tables and illustrations.

The expressivities are indicated as percentages (always in relation to 68 patients) in the first table (see also Table 10).

Graphic 5 elucidates which symptoms were ‘very severe’ at the start of treatment. In particular, ‘tender points’ (72.1% of patients with severe expressivity), muscle pains (66.2%) as well as ‘back pains’ and ‘poor night sleep’ (each with 63.2%) are to be mentioned here.

In the end, the symptom score for all symptoms was established for better comparability. This mean value of the respective symptom was calculated from the evaluations 0=nonexistent, 1=less, 2=moderate and 3=severe (Table 11).

## 3.1.1. Expressivity of symptoms at start of treatment (in percent)

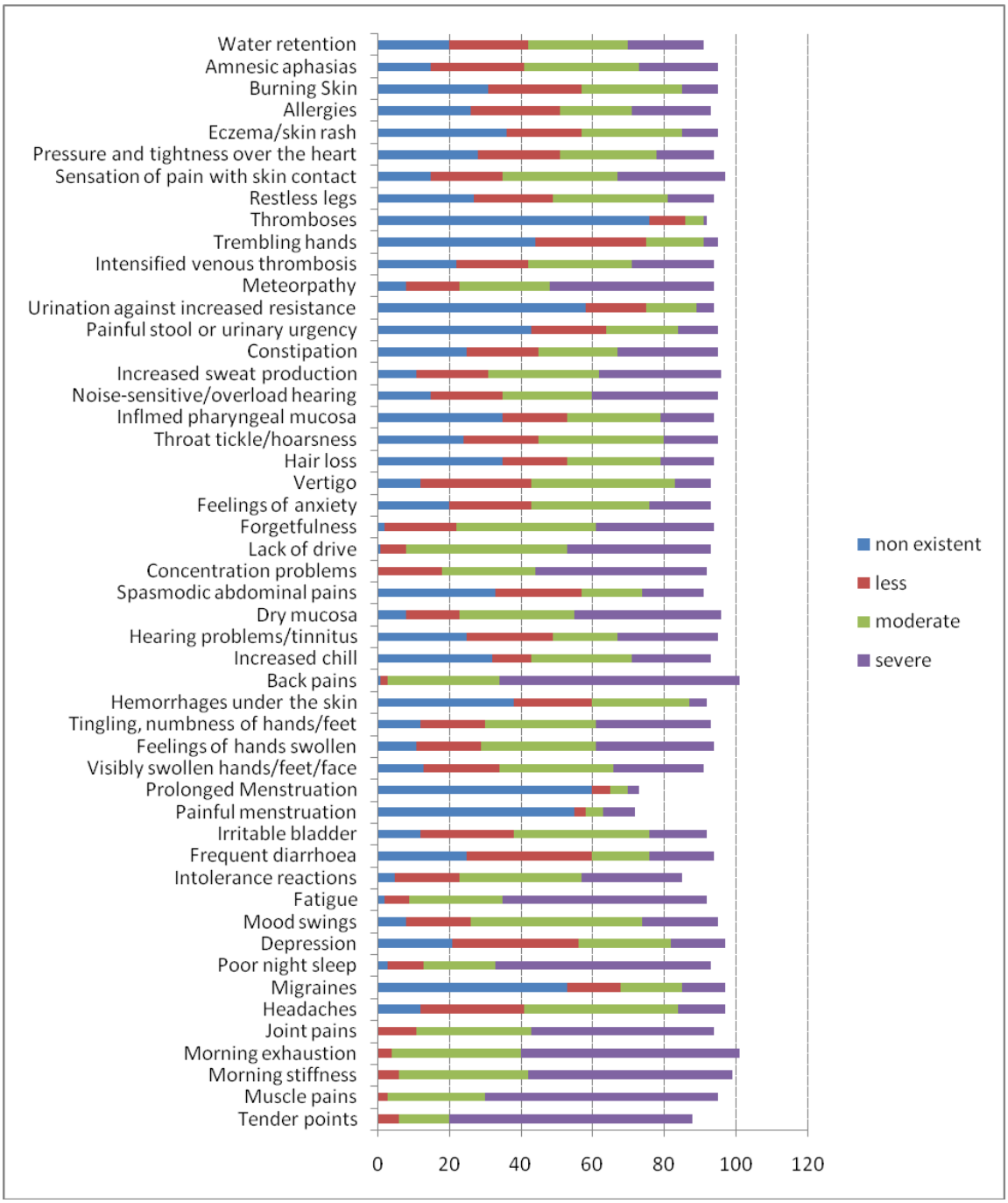
Expressivity of concomitant symptoms at start of treatment [percentages]

| | Nonexistent | Less | Moderate | Severe | No data |
|---|---|---|---|---|---|
| Tender points | | 7.4 | 14.7 | 72.1 | 5.9 |
| Muscle pains | | 2.9 | 29.4 | 66.2 | 1.5 |
| Morning stiffness | | 5.9 | 36.8 | 57.4 | |
| Morning exhaustion | | 4.4 | 35.3 | 60.3 | |
| Joint pains | | 11.8 | 33.8 | 54.4 | |
| Headaches | 11.8 | 29.4 | 44.1 | 13.2 | 1.5 |
| Migraines | 54.4 | 16.2 | 16.2 | 11.8 | 1.5 |
| Poor night sleep | 2.9 | 11.8 | 22.1 | 63.2 | |
| Depressions | 22.1 | 36.8 | 27.9 | 13.2 | |
| Mood swings | 8.8 | 19.1 | 50.0 | 22.1 | |
| Fatigue | 1.5 | 7.4 | 27.9 | 60.3 | 2.9 |
| Intolerance reactions | 5.9 | 19.1 | 35.3 | 29.4 | 10.3 |
| Frequent diarrhea | 26.5 | 36.8 | 17.6 | 19.1 | |
| Irritable bladder | 13.2 | 27.9 | 39.7 | 17.6 | 1.5 |
| Painful menstruation | 58.8 | 4.4 | 5.9 | 8.8 | 22.1 |
| Prolonged menstruation | 63.2 | 5.9 | 5.9 | 2.9 | 22.1 |
| Visibly swollen hands/feet/face | 14.7 | 22.1 | 33.8 | 26.5 | 2.9 |
| Feeling as if hands swollen | 11.8 | 19.1 | 33.8 | 35.3 | |
| Tingling, numbness of hands/feet | 13.2 | 19.1 | 32.4 | 33.8 | 1.5 |
| Hemorrhages under the skin | 39.7 | 23.5 | 29.4 | 5.9 | 1.5 |
| Back pains | 1.5 | 2.9 | 32.4 | 63.2 | |
| Increased chill | 33.8 | 11.8 | 29.4 | 23.5 | 1.5 |
| Hearing problems/tinnitus | 26.5 | 25.0 | 19.1 | 29.4 | |
| Dry mucosae | 8.8 | 14.7 | 33.8 | 42.6 | |
| Spasmodic abdominal pains | 35.3 | 25.0 | 19.1 | 17.6 | 2.9 |
| Concentration problems | | 19.1 | 27.9 | 51.5 | 1.5 |
| Lack of drive | 1.5 | 7.4 | 47.1 | 42.6 | 1.5 |
| Forgetfulness | 2.9 | 20.6 | 41.2 | 35.3 | |
| Feelings of anxiety | 20.6 | 25.0 | 35.3 | 17.6 | 1.5 |
| Vertigo | 13.2 | 32.4 | 42.6 | 10.3 | 1.5 |
| Hair loss | 36.8 | 19.1 | 27.9 | 16.2 | |
| Throat tickle/hoarseness | 25.0 | 22.1 | 36.8 | 16.2 | |
| Inflamed pharyngeal mucosa | 36.8 | 29.4 | 23.5 | 8.8 | 1.5 |
| Noise-sensitive/overloud hearing | 16.2 | 20.6 | 26.5 | 36.8 | |
| Increased sweat production | 11.8 | 20.6 | 32.4 | 35.3 | |
| Constipation | 26.5 | 20.6 | 23.5 | 29.4 | |
| Painful stool or urinary urgency | 45.6 | 22.1 | 20.6 | 11.8 | |
| Urination against increased resistance | 61.8 | 19.1 | 14.7 | 4.4 | |
| Meteoropathy | 8.8 | 16.2 | 26.5 | 48.5 | |
| Intensified venous thrombosis | 23.5 | 20.6 | 30.9 | 23.5 | 1.5 |
| Trembling hands | 47.1 | 32.4 | 16.2 | 4.4 | |
| Thromboses | 80.9 | 10.3 | 5.9 | 1.5 | 1.5 |
| Restless legs | 27.9 | 23.5 | 33.8 | 13.2 | 1.5 |
| Sensation of pain with skin contact | 16.2 | 19.1 | 33.8 | 30.9 | |
| Pressure & tightness over the heart | 29.4 | 25.0 | 29.4 | 16.2 | |
| Eczema/skin rash | 38.2 | 22.1 | 29.4 | 8.8 | 1.5 |
| Allergies | 27.9 | 26.5 | 22.1 | 23.5 | |
| Burning skin | 32.4 | 27.9 | 29.4 | 10.3 | |
| Amnesic aphasias | 14.7 | 27.9 | 33.8 | 23.5 | |
| Water retentions | 20.6 | 23.5 | 30.9 | 23.5 | 1.5 |

Table 10

### 3.1.2. Expressivity of symptoms at start of treatment

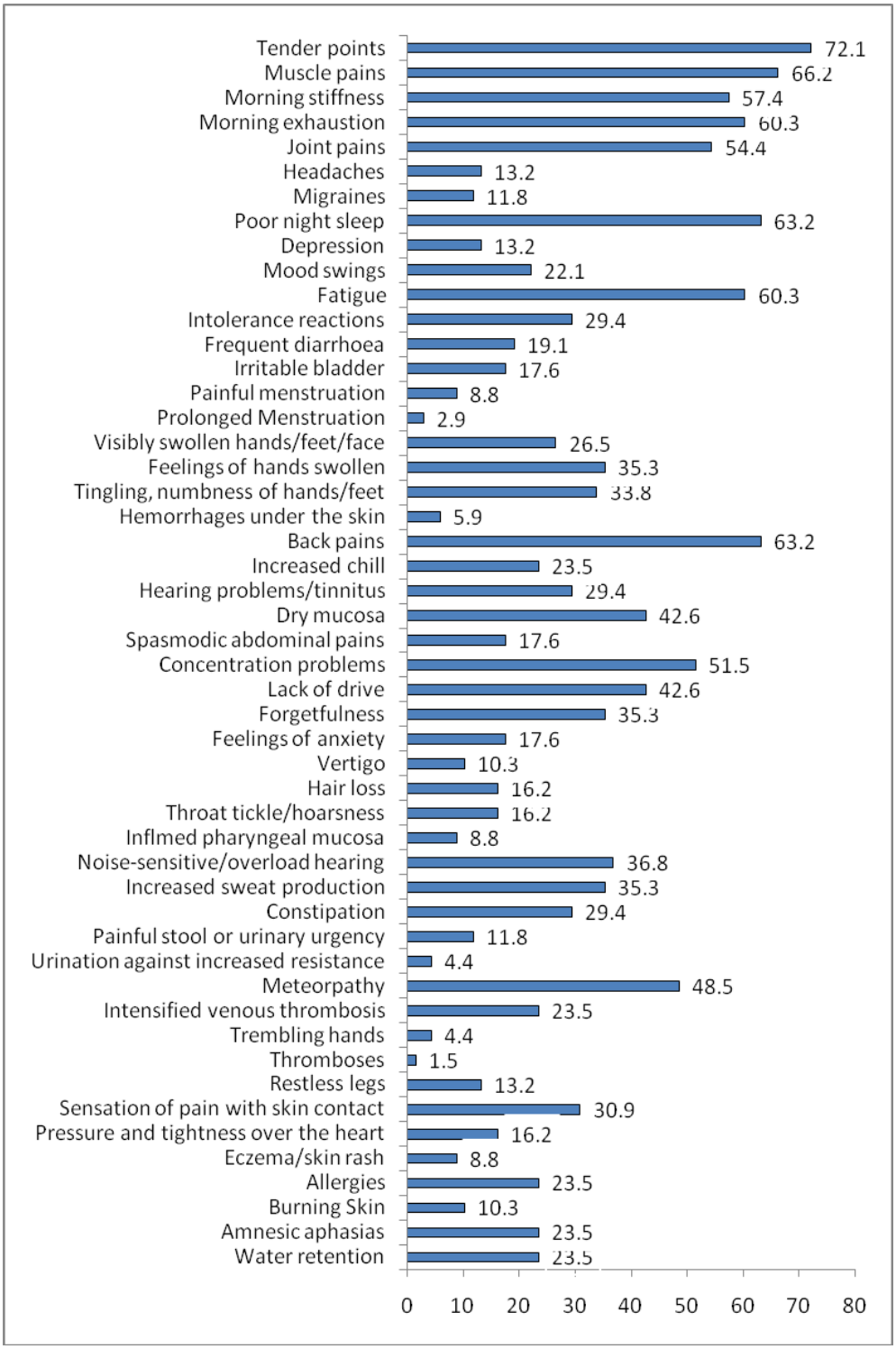
Indicated is the percentage of 68 patients in which the respective symptom at the time of the start of treatment was nonexistent, less, moderate or very severe. On account of the missing details (above all with questions regarding menstruation), the addition of patient details does not always result in 100%.




Graphic 4

### 3.1.3. Severe expressivity of symptoms at start of treatment

Indicated is the percentage of 68 patients in which the respective symptom at the time of the start of the treatment was very severe.




Graphic 5

## 3.1.4. Symptom score at start of treatment

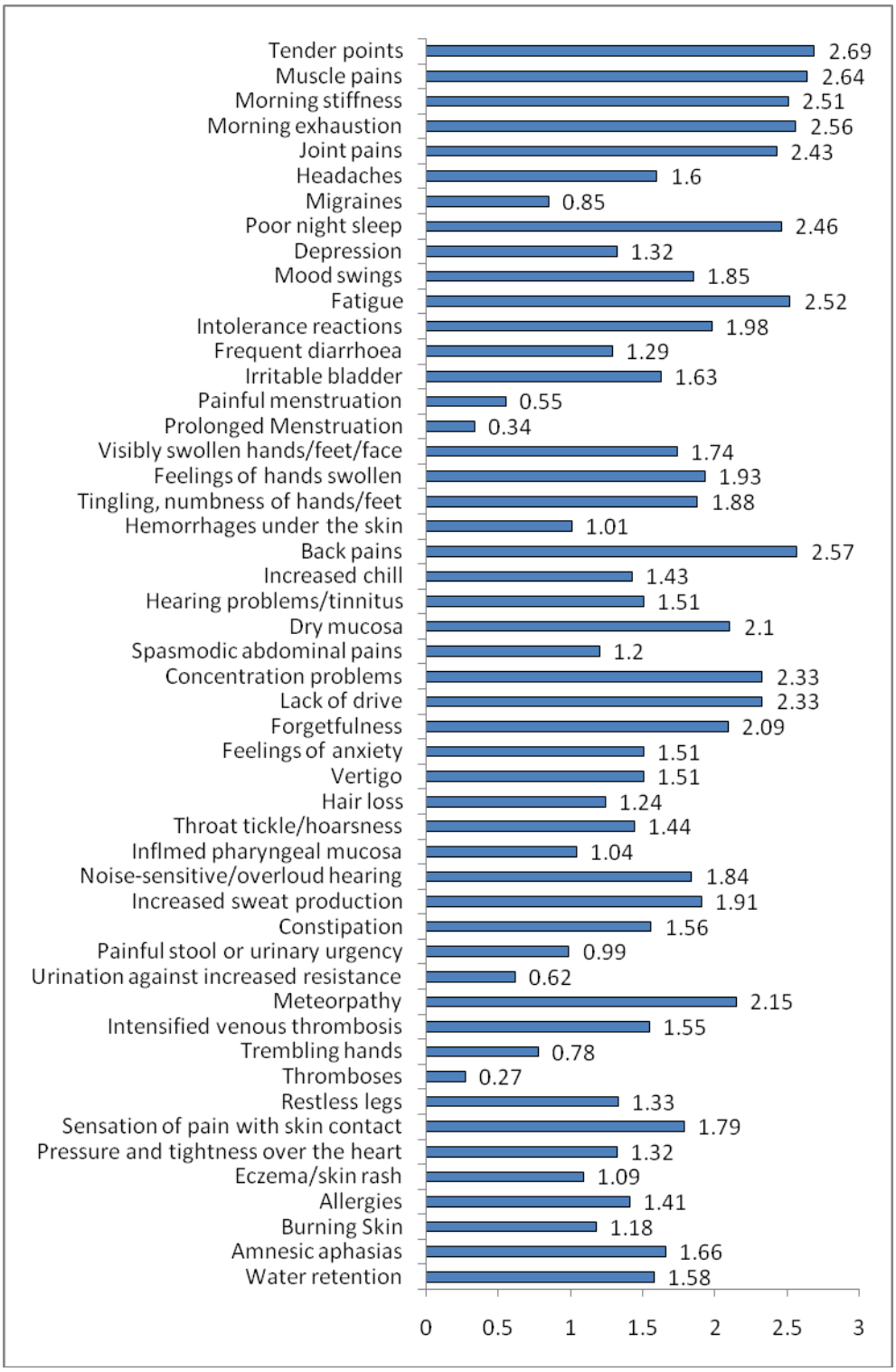
Indicated is the mean value of the respective symptom, calculated from the evaluations 0=nonexistent, 1=less, 2=moderate and 3=severe.

**Symptom score during admission visit**

| Symptom | Mean value | Standard Dev. | Median | Valid N |
|---|---|---|---|---|
| Tender points | 2.69 | 0.61 | 3 | N=64 |
| Muscle pains | 2.64 | 0.54 | 3 | N=67 |
| Morning stiffness | 2.51 | 0.61 | 3 | N=68 |
| Morning exhaustion | 2.56 | 0.58 | 3 | N=68 |
| Joint pains | 2.43 | 0.70 | 3 | N=68 |
| Headaches | 1.60 | 0.87 | 2 | N=67 |
| Migraines | 0.85 | 1.09 | 0 | N=67 |
| Poor night sleep | 2.46 | 0.82 | 3 | N=68 |
| Depressions | 1.32 | 0.97 | 1 | N=68 |
| Mood swings | 1.85 | 0.87 | 2 | N=68 |
| Fatigue | 2.52 | 0.71 | 3 | N=66 |
| Intolerance reactions | 1.98 | 0.90 | 2 | N=61 |
| Frequent diarrhea | 1.29 | 1.07 | 1 | N=68 |
| Irritable bladder | 1.63 | 0.93 | 2 | N=67 |
| Painful menstruation | 0.55 | 1.05 | 0 | N=53 |
| Prolonged menstruation | 0.34 | 0.78 | 0 | N=53 |
| Visibly swollen hands/feet/face | 1.74 | 1.03 | 2 | N=66 |
| Feeling as if hands swollen | 1.93 | 1.01 | 2 | N=68 |
| Tingling. numbness of hands/feet | 1.88 | 1.04 | 2 | N=67 |
| Hemorrhages under the skin | 1.01 | 0.98 | 1 | N=67 |
| Back pains | 2.57 | 0.63 | 3 | N=68 |
| Increased chill | 1.43 | 1.20 | 2 | N=67 |
| Hearing problems/tinnitus | 1.51 | 1.18 | 1 | N=68 |
| Dry mucosae | 2.10 | 0.96 | 2 | N=68 |
| Spasmodic abdominal pains | 1.20 | 1.13 | 1 | N=66 |
| Concentration problems | 2.33 | 0.79 | 3 | N=67 |
| Lack of drive | 2.33 | 0.68 | 2 | N=67 |
| Forgetfulness | 2.09 | 0.82 | 2 | N=68 |
| Feelings of anxiety | 1.51 | 1.02 | 2 | N=67 |
| Vertigo | 1.51 | 0.86 | 2 | N=67 |
| Hair loss | 1.24 | 1.12 | 1 | N=68 |
| Throat tickle/hoarseness | 1.44 | 1.04 | 2 | N=68 |
| Inflamed pharyngeal mucosa | 1.04 | 0.99 | 1 | N=67 |
| Noise-sensitive/overloud hearing | 1.84 | 1.10 | 2 | N=68 |
| Increased sweat production | 1.91 | 1.02 | 2 | N=68 |
| Constipation | 1.56 | 1.18 | 2 | N=68 |
| Painful stool or urinary urgency | 0.99 | 1.07 | 1 | N=68 |
| Urination against increased resistance | 0.62 | 0.90 | 0 | N=68 |
| Meteoropathy | 2.15 | 1.00 | 2 | N=68 |
| intensified venous thrombosis | 1.55 | 1.10 | 2 | N=67 |
| Trembling hands | 0.78 | 0.88 | 1 | N=68 |
| Thromboses | 0.27 | 0.64 | 0 | N=67 |
| Restless legs | 1.33 | 1.04 | 1 | N=67 |
| Sensation of pain with skin contact | 1.79 | 1.06 | 2 | N=68 |
| Pressure & tightness over the heart | 1.32 | 1.07 | 1 | N=68 |
| Eczema/skin rash | 1.09 | 1.03 | 1 | N=67 |
| Allergies | 1.41 | 1.14 | 1 | N=68 |
| Burning skin | 1.18 | 1.01 | 1 | N=68 |
| Amnesic aphasias | 1.66 | 1.00 | 2 | N=68 |
| Water retentions | 1.58 | 1.08 | 2 | N=67 |

Table 11

## Symptom score at start of treatment




Graphic 6

## 3.2. Detection of specific IgG against food

On average, the patients had 47.2 ± 11.4 food reactions (median: 50 reactions). Of these, an average of 9.3 ± 11.7 reactions was very severe (severity 3 and 4). It is conspicuous that the total number of reactions with the fibromyalgia patients evaluated here is approx. 20% higher than in patients with comparable age structure who participated in parallel implemented application observation with other indication emphases.

### 3.2.1. Total number of food reactions

**Number of food reactions according to sex**

**Number of all food reactions**

| Sex | Mean Value | Standard Deviation | Minimum | Maximum | 25th percentile | Median | 75th percentile | Valid N |
|---|---|---|---|---|---|---|---|---|
| Male | 47.6 | 8.5 | 32.0 | 61.0 | 42.5 | 50.0 | 51.5 | N=8 |
| Female | 47.1 | 11.8 | 20.0 | 70.0 | 41.0 | 50.0 | 53.0 | N=59 |
| Total | 47.2 | 11.4 | 20.0 | 70.0 | 41.0 | 50.0 | 52.0 | N=67 |

Table 12

### 3.2.2. Number of food reactions with severity 3 or 4

**Number of food reactions with severity 3 or 4 according to sex**

**Number of all food reactions with severity 3 or 4**

| Sex | Mean Value | Standard Deviation | Minimum | Maximum | 25th percentile | Median | 75th percentile | Valid N |
|---|---|---|---|---|---|---|---|---|
| Male | 7.1 | 8.3 | 1.0 | 27.0 | 2.5 | 5.0 | 6.8 | N=8 |
| Female | 9.6 | 12.2 | 1.0 | 70.0 | 4.0 | 7.0 | 12.0 | N=55 |
| Total | 9.3 | 11.7 | 1.0 | 70.0 | 4.0 | 6.0 | 11.0 | N=63 |

Table 13

## 3.3. Symptom expressivity in the course

The expressivity of 50 predetermined symptoms should be assessed at all documentation points with the help of a 4-step scale ranging from 0=nonexistent via 1=less, 2=moderate to 3=severe.

The expressivity of 50 predetermined symptoms in the course of the 8-week observation period has been processed in the following tables and illustrations.

In the first 4 tables, the distribution of expressivities is presented after 2, 4, 6 and 8 weeks for all symptoms. The results after 8 weeks have also been graphically depicted (Graphic 7). In comparison with tables and illustrations in Section 5 it becomes clear how severely the expressivity of the individual symptoms has diminished in the course of 8 weeks. For instance, Graphic 8 shows the percentage of patients in which the symptom ‘tender points’ was very severe dropped from 72.1% at the start of treatment to 33.8% after 8 weeks. A few other examples: ‘muscle pains’ from 66.2% to 25%, ‘poor night sleep’ from 63.2% to 22.1% and ‘joint pains’ from 54.4% to 29.4%.

## 3.3.1. Expressivity of symptoms after 2 weeks (in percent)

**Expressivity of symptoms after 2 weeks [in percent]**

| | Nonexistent | Less | Moderate | Severe | No data |
|---|---|---|---|---|---|
| Tender points | 1.5 | 10.3 | 39.7 | 45.6 | 2.9 |
| Muscle pains | 1.5 | 16.2 | 41.2 | 41.2 | |
| Morning stiffness | 1.5 | 16.2 | 45.6 | 35.3 | 1.5 |
| Morning exhaustion | 4.4 | 17.6 | 36.8 | 41.2 | |
| Joint pains | 2.9 | 26.5 | 32.4 | 38.2 | |
| Headaches | 25.0 | 30.9 | 38.2 | 4.4 | 1.5 |
| Migraines | 72.1 | 7.4 | 13.2 | 5.9 | 1.5 |
| Poor night sleep | 1.5 | 26.5 | 38.2 | 33.8 | |
| Depressions | 30.9 | 33.8 | 23.5 | 10.3 | 1.5 |
| Mood swings | 13.2 | 35.5 | 33.8 | 16.2 | 1.5 |
| Fatigue | 4.4 | 20.6 | 38.2 | 36.8 | |
| Intolerance reactions | 23.5 | 35.3 | 36.5 | 11.8 | 2.9 |
| Frequent diarrhea | 52.9 | 20.6 | 16.2 | 10.3 | |
| Irritable bladder | 32.4 | 20.6 | 36.8 | 10.3 | |
| Painful menstruation | 63.2 | 4.4 | 4.4 | 2.9 | 25.0 |
| Prolonged menstruation | 64.7 | 4.4 | 2.9 | 1.5 | 26.5 |
| Visibly swollen hands/feet/face | 25.0 | 29.4 | 32.4 | 11.8 | 1.5 |
| Feeling as if hands swollen | 20.6 | 26.5 | 36.8 | 16.2 | |
| Tingling, numbness of hands/feet | 20.6 | 25.0 | 30.9 | 22.1 | 1.5 |
| Hemorrhages under the skin | 47.1 | 20.6 | 26.5 | 1.5 | 4.4 |
| Back pains | 1.5 | 32.2 | 36.8 | 48.5 | |
| Increased chill | 38.2 | 11.8 | 30.9 | 17.6 | 1.5 |
| Hearing problems/tinnitus | 27.9 | 33.8 | 25.0 | 13.2 | |
| Dry mucosae | 13.2 | 25.0 | 35.3 | 26.5 | |
| Spasmodic abdominal pains | 50.0 | 23.5 | 16.2 | 8.8 | 1.5 |
| Concentration problems | 1.5 | 23.5 | 38.2 | 36.8 | |
| Lack of drive | 4.4 | 22.1 | 45.6 | 27.9 | |
| Forgetfulness | 2.9 | 29.4 | 36.8 | 30.9 | |
| Feelings of anxiety | 29.4 | 29.4 | 30.9 | 10.3 | |
| Vertigo | 25.0 | 41.2 | 23.5 | 10.3 | |
| Hair loss | 41.2 | 27.9 | 16.2 | 11.8 | 2.9 |
| Throat tickle/hoarseness | 35.3 | 29.4 | 26.5 | 8.8 | |
| Inflamed pharyngeal mucosa | 52.9 | 22.1 | 17.6 | 7.4 | |
| Noise-sensitive/overloud hearing | 22.1 | 20.6 | 29.4 | 26.5 | 1.5 |
| Increased sweat production | 19.1 | 20.6 | 29.4 | 29.4 | 1.5 |
| Constipation | 45.6 | 8.8 | 29.4 | 13.2 | 2.9 |
| Painful stool or urinary urgency | 54.4 | 30.9 | 8.8 | 5.9 | |
| Urination against increased resistance | 61.8 | 23.5 | 11.8 | 1.5 | 1.5 |
| Meteoropathy | 13.2 | 19.1 | 36.8 | 30.9 | |
| Intensified venous thrombosis | 25.0 | 27.9 | 25.0 | 20.6 | 1.5 |
| Trembling hands | 55.9 | 27.9 | 14.7 | 1.5 | |
| Thromboses | 82.4 | 7.4 | 5.9 | 1.5 | 2.9 |
| Restless legs | 32.4 | 33.8 | 25.0 | 8.8 | |
| Sensation of pain with skin contact | 22.1 | 26.5 | 32.4 | 19.1 | |
| Pressure & tightness over the heart | 39.7 | 25.0 | 25.0 | 10.3 | |
| Eczema/skin rash | 52.9 | 23.5 | 17.6 | 5.9 | |
| Allergies | 39.7 | 25.0 | 22.1 | 11.8 | 1.5 |
| Burning skin | 47.1 | 26.5 | 22.1 | 4.4 | |
| Amnesic aphasias | 17.6 | 26.5 | 32.4 | 23.5 | |
| Water retentions | 29.4 | 25.0 | 36.8 | 8.8 | |

Percentages values in relation to all 68 patients

Table 14

## 3.3.2. Expressivity of symptoms after 4 weeks (in percent)

**Expressivity of symptoms after 4 weeks [in percent]**

| | Nonexistent | Less | Moderate | Severe | No data |
|---|---|---|---|---|---|
| Tender points | 2.9 | 19.1 | 33.8 | 41.2 | 2.9 |
| Muscle pains | 1.5 | 19.1 | 44.1 | 33.8 | 1.5 |
| Morning stiffness | 2.9 | 22.1 | 42.6 | 32.4 | |
| Morning exhaustion | 10.3 | 22.1 | 33.8 | 32.4 | 1.5 |
| Joint pains | 4.4 | 29.4 | 35.3 | 29.4 | 1.5 |
| Headaches | 32.4 | 32.4 | 26.5 | 7.4 | 1.5 |
| Migraines | 72.1 | 10.3 | 10.3 | 5.9 | 1.5 |
| Poor night sleep | 4.4 | 23.5 | 47.1 | 25.0 | |
| Depressions | 35.3 | 35.3 | 20.6 | 7.4 | 1.5 |
| Mood swings | 19.1 | 44.1 | 25.0 | 10.3 | 1.5 |
| Fatigue | 5.9 | 22.1 | 47.1 | 25.0 | |
| Intolerance reactions | 22.1 | 47.1 | 16.2 | 11.8 | 2.9 |
| Frequent diarrhea | 52.9 | 20.6 | 16.2 | 10.3 | |
| Irritable bladder | 39.7 | 25.0 | 27.9 | 7.4 | |
| Painful menstruation | 63.2 | 4.4 | 1.5 | 2.9 | 27.9 |
| Prolonged menstruation | 66.2 | 1.5 | 2.9 | 1.5 | 27.9 |
| Visibly swollen hands/feet/face | 30.9 | 32.4 | 29.4 | 5.9 | 1.5 |
| Feeling as if hands swollen | 26.5 | 26.5 | 41.2 | 5.9 | |
| Tingling, numbness of hands/feet | 29.4 | 26.5 | 27.9 | 16.2 | |
| Hemorrhages under the skin | 51.5 | 26.5 | 17.6 | 2.9 | 1.5 |
| Back pains | | 20.6 | 44.1 | 35.3 | |
| Increased chill | 41.2 | 17.6 | 29.4 | 10.3 | 1.5 |
| Hearing problems/tinnitus | 30.9 | 30.9 | 26.5 | 11.8 | |
| Dry mucosae | 14.7 | 23.5 | 35.3 | 26.5 | |
| Spasmodic abdominal pains | 51.5 | 25.0 | 14.7 | 7.4 | 1.5 |
| Concentration problems | 2.9 | 33.8 | 33.8 | 29.4 | |
| Lack of drive | 4.4 | 32.4 | 45.6 | 16.2 | 1.5 |
| Forgetfulness | 8.8 | 32.4 | 35.3 | 23.5 | |
| Feelings of anxiety | 36.8 | 32.4 | 23.5 | 7.4 | |
| Vertigo | 32.4 | 36.8 | 20.6 | 10.3 | |
| Hair loss | 45.6 | 23.5 | 19.1 | 8.8 | 2.9 |
| Throat tickle/hoarseness | 41.2 | 32.4 | 17.6 | 8.8 | |
| Inflamed pharyngeal mucosa | 57.4 | 14.7 | 16.2 | 10.3 | 1.5 |
| Noise-sensitive/overloud hearing | 22.1 | 23.5 | 26.5 | 27.9 | |
| Increased sweat production | 22.1 | 25.0 | 30.9 | 22.1 | |
| Constipation | 48.5 | 19.1 | 17.6 | 14.7 | |
| Painful stool or urinary urgency | 60.3 | 25.0 | 5.9 | 8.8 | |
| Urination against increased resistance | 73.5 | 17.6 | 5.9 | 2.9 | |
| Meteoropathy | 17.6 | 23.5 | 32.4 | 26.5 | |
| Intensified venous thrombosis | 29.4 | 29.4 | 23.5 | 16.2 | 1.5 |
| Trembling hands | 55.9 | 27.9 | 13.2 | 2.9 | |
| Thromboses | 86.8 | 5.9 | 4.4 | | 2.9 |
| Restless legs | 36.8 | 27.9 | 25.0 | 10.3 | |
| Sensation of pain with skin contact | 30.9 | 23.5 | 30.9 | 14.7 | |
| Pressure & tightness over the heart | 42.6 | 29.4 | 19.1 | 7.4 | 1.5 |
| Eczema/skin rash | 57.4 | 25.0 | 10.3 | 7.4 | |
| Allergies | 45.6 | 33.8 | 13.2 | 7.4 | |
| Burning skin | 48.5 | 32.4 | 16.2 | 2.9 | |
| Amnesic aphasias | 22.1 | 23.5 | 32.4 | 22.1 | |
| Water retentions | 30.9 | 41.2 | 23.5 | 4.4 | |

Percentages values in relation to all 68 patients

Table 15

## 3.3.3. Expressivity of symptoms after 6 weeks (in percent)

**Expressivity of symptoms after 6 weeks [in percent]**

| | Nonexistent | Less | Moderate | Severe | No data |
|---|---|---|---|---|---|
| Tender points | 2.9 | 20.6 | 39.7 | 33.8 | 2.9 |
| Muscle pains | 2.9 | 20.6 | 45.6 | 30.9 | |
| Morning stiffness | 4.4 | 30.9 | 39.7 | 25.0 | |
| Morning exhaustion | 5.9 | 33.8 | 32.4 | 27.9 | |
| Joint pains | 4.4 | 27.9 | 36.8 | 29.4 | 1.5 |
| Headaches | 32.4 | 32.4 | 29.4 | 4.4 | 1.5 |
| Migraines | 73.5 | 14.7 | 5.9 | 1.5 | 4.4 |
| Poor night sleep | 7.4 | 30.9 | 32.4 | 27.9 | 1.5 |
| Depressions | 42.6 | 27.9 | 16.2 | 10.3 | 2.9 |
| Mood swings | 26.5 | 35.3 | 23.5 | 13.2 | 1.5 |
| Fatigue | 7.4 | 33.8 | 32.4 | 26.5 | |
| Intolerance reactions | 26.5 | 44.1 | 16.2 | 8.8 | 4.4 |
| Frequent diarrhea | 57.4 | 20.6 | 13.2 | 8.8 | |
| Irritable bladder | 47.1 | 22.1 | 27.9 | 2.9 | |
| Painful menstruation | 67.6 | 2.9 | | 2.9 | 26.5 |
| Prolonged menstruation | 67.6 | | 4.4 | 1.5 | 26.5 |
| Visibly swollen hands/feet/face | 29.4 | 38.2 | 20.6 | 10.3 | 1.5 |
| Feeling as if hands swollen | 20.6 | 33.8 | 30.9 | 13.2 | 1.5 |
| Tingling, numbness of hands/feet | 29.4 | 30.9 | 29.4 | 10.3 | |
| Hemorrhages under the skin | 50.0 | 32.4 | 11.8 | 5.9 | |
| Back pains | 1.5 | 26.5 | 32.4 | 39.7 | |
| Increased chill | 39.7 | 23.5 | 20.6 | 11.8 | 4.4 |
| Hearing problems/tinnitus | 36.8 | 26.5 | 20.6 | 16.2 | |
| Dry mucosae | 16.2 | 30.9 | 32.4 | 20.6 | |
| Spasmodic abdominal pains | 55.9 | 29.4 | 10.3 | 2.9 | 1.5 |
| Concentration problems | 8.8 | 29.4 | 32.4 | 29.4 | |
| Lack of drive | 7.4 | 39.7 | 32.4 | 20.6 | |
| Forgetfulness | 7.4 | 30.9 | 38.2 | 23.5 | |
| Feelings of anxiety | 41.2 | 32.4 | 17.6 | 8.8 | |
| Vertigo | 32.4 | 35.3 | 27.9 | 4.4 | |
| Hair loss | 42.6 | 29.4 | 19.1 | 7.4 | 1.5 |
| Throat tickle/hoarseness | 48.5 | 26.5 | 17.6 | 7.4 | |
| Inflamed pharyngeal mucosa | 55.9 | 23.5 | 8.8 | 10.3 | 1.5 |
| Noise-sensitive/overloud hearing | 25.0 | 26.5 | 23.5 | 25.0 | |
| Increased sweat production | 25.0 | 25.0 | 25.0 | 25.0 | |
| Constipation | 48.5 | 27.9 | 11.8 | 10.3 | 1.5 |
| Painful stool or urinary urgency | 66.2 | 22.1 | 7.4 | 4.4 | |
| Urination against increased resistance | 76.5 | 17.6 | 2.9 | 2.9 | |
| Meteoropathy | 13.2 | 33.8 | 26.5 | 26.5 | |
| Intensified venous thrombosis | 30.9 | 23.5 | 29.4 | 13.2 | 2.9 |
| Trembling hands | 61.8 | 19.1 | 16.2 | 2.9 | |
| Thromboses | 85.3 | 4.4 | 5.9 | | 4.4 |
| Restless legs | 39.7 | 25.0 | 23.5 | 11.8 | |
| Sensation of pain with skin contact | 30.9 | 30.9 | 29.4 | 8.8 | |
| Pressure & tightness over the heart | 52.9 | 22.1 | 20.6 | 4.4 | |
| Eczema/skin rash | 55.9 | 27.9 | 11.8 | 4.4 | |
| Allergies | 52.9 | 26.5 | 17.6 | 2.9 | |
| Burning skin | 51.5 | 35.3 | 10.3 | 2.9 | |
| Amnesic aphasias | 20.6 | 30.9 | 32.4 | 16.2 | |
| Water retentions | 30.9 | 38.2 | 27.9 | 2.9 | |

Percentages values in relation to all 68 patients

Table 16

## 3.3.4. Expressivity of symptoms after 8 weeks

**Expressivity of symptoms after 8 weeks [in percent]**

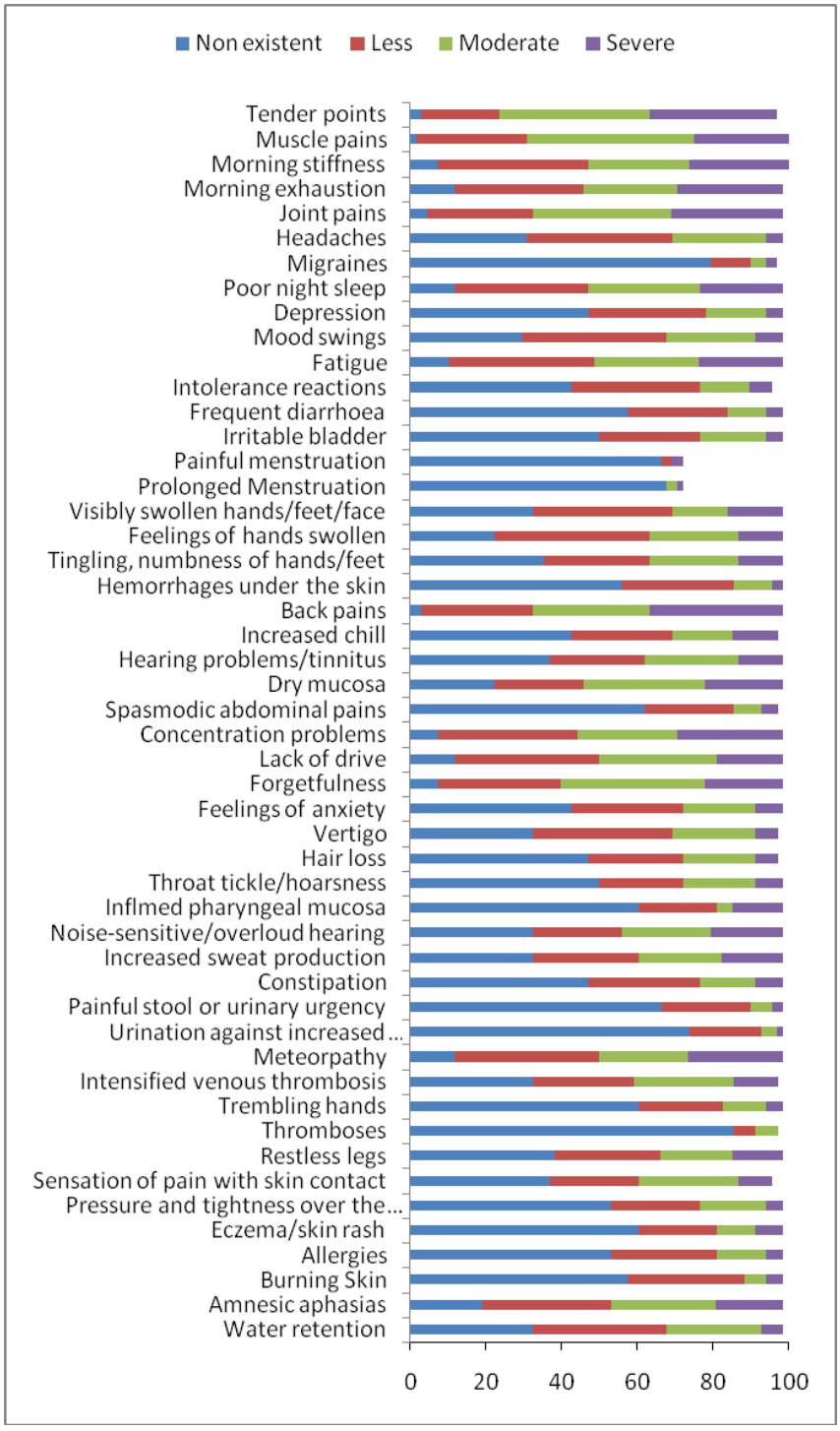
| | Nonexistent | Less | Moderate | Severe | No data |
|---|---|---|---|---|---|
| Tender points | 2.9 | 20.6 | 39.7 | 33.8 | 2.9 |
| Muscle pains | 1.5 | 29.4 | 44.1 | 25.0 | |
| Morning stiffness | 7.4 | 39.7 | 26.5 | 26.5 | |
| Morning exhaustion | 11.8 | 33.8 | 25.0 | 27.9 | 1.5 |
| Joint pains | 4.4 | 27.9 | 36.8 | 29.4 | 1.5 |
| Headaches | 30.9 | 38.2 | 25.0 | 4.4 | 1.5 |
| Migraines | 79.4 | 10.3 | 4.4 | 2.9 | 2.9 |
| Poor night sleep | 11.8 | 35.3 | 29.4 | 22.1 | 1.5 |
| Depressions | 47.1 | 30.9 | 16.2 | 4.4 | 1.5 |
| Mood swings | 29.4 | 38.2 | 23.5 | 7.4 | 1.5 |
| Fatigue | 10.3 | 38.2 | 27.9 | 22.1 | 1.5 |
| Intolerance reactions | 42.6 | 33.8 | 13.2 | 5.9 | 4.4 |
| Frequent diarrhea | 57.4 | 26.5 | 10.3 | 4.4 | 1.5 |
| Irritable bladder | 50.0 | 26.5 | 17.6 | 4.4 | 1.5 |
| Painful menstruation | 66.2 | 2.9 | | 2.9 | 27.9 |
| Prolonged menstruation | 67.6 | | 2.9 | 1.5 | 27.9 |
| Visibly swollen hands/feet/face | 32.4 | 36.8 | 14.7 | 14.7 | 1.5 |
| Feeling as if hands swollen | 22.1 | 41.2 | 23.5 | 11.8 | 1.5 |
| Tingling, numbness of hands/feet | 35.3 | 27.9 | 23.5 | 11.8 | 1.5 |
| Hemorrhages under the skin | 55.9 | 29.4 | 10.3 | 2.9 | 1.5 |
| Back pains | 2.9 | 29.4 | 30.9 | 35.3 | 1.5 |
| Increased chill | 42.6 | 26.5 | 16.2 | 11.8 | 2.9 |
| Hearing problems/tinnitus | 36.8 | 25.0 | 25.0 | 11.8 | 1.5 |
| Dry mucosae | 22.1 | 23.5 | 32.4 | 20.6 | 1.5 |
| Spasmodic abdominal pains | 61.8 | 23.5 | 7.4 | 4.4 | 2.9 |
| Concentration problems | 7.4 | 36.8 | 26.5 | 27.9 | 1.5 |
| Lack of drive | 11.8 | 38.2 | 30.9 | 17.6 | 1.5 |
| Forgetfulness | 7.4 | 32.4 | 38.2 | 20.6 | 1.5 |
| Feelings of anxiety | 42.6 | 29.4 | 19.1 | 7.4 | 1.5 |
| Vertigo | 32.4 | 36.8 | 22.1 | 5.9 | 2.9 |
| Hair loss | 47.1 | 25.0 | 19.1 | 5.9 | 2.9 |
| Throat tickle/hoarseness | 50.0 | 22.1 | 19.1 | 7.4 | 1.5 |
| Inflamed pharyngeal mucosa | 60.3 | 20.6 | 4.4 | 13.2 | 1.5 |
| Noise-sensitive/overloud hearing | 32.4 | 23.5 | 23.5 | 19.1 | 1.5 |
| Increased sweat production | 32.4 | 27.9 | 22.1 | 16.2 | 1.5 |
| Constipation | 47.1 | 29.4 | 14.7 | 7.4 | 1.5 |
| Painful stool or urinary urgency | 66.2 | 23.5 | 5.9 | 2.9 | 1.5 |
| Urination against increased resistance | 73.5 | 19.1 | 4.4 | 1.5 | 1.5 |
| Meteoropathy | 11.8 | 38.2 | 23.5 | 25.0 | 1.5 |
| Intensified venous thrombosis | 32.4 | 26.5 | 26.5 | 11.8 | 2.9 |
| Trembling hands | 60.3 | 22.1 | 11.8 | 4.4 | 1.5 |
| Thromboses | 85.3 | 5.9 | 5.9 | | 2.9 |
| Restless legs | 38.2 | 27.9 | 19.1 | 13.2 | 1.5 |
| Sensation of pain with skin contact | 36.8 | 23.5 | 26.5 | 8.8 | 4.4 |
| Pressure & tightness over the heart | 52.9 | 23.5 | 17.6 | 4.4 | 1.5 |
| Eczema/skin rash | 60.3 | 20.6 | 10.3 | 7.4 | 1.5 |
| Allergies | 52.9 | 27.9 | 13.2 | 4.4 | 1.5 |
| Burning skin | 57.4 | 30.9 | 5.9 | 4.4 | 1.5 |
| Amnesic aphasias | 19.1 | 33.8 | 27.9 | 17.6 | 1.5 |
| Water retentions | 32.4 | 35.3 | 25.0 | 5.9 | 1.5 |

Percentages values in relation to all 68 patients

Table 17

### 3.3.4.1. Expressivity of symptoms after 8 weeks

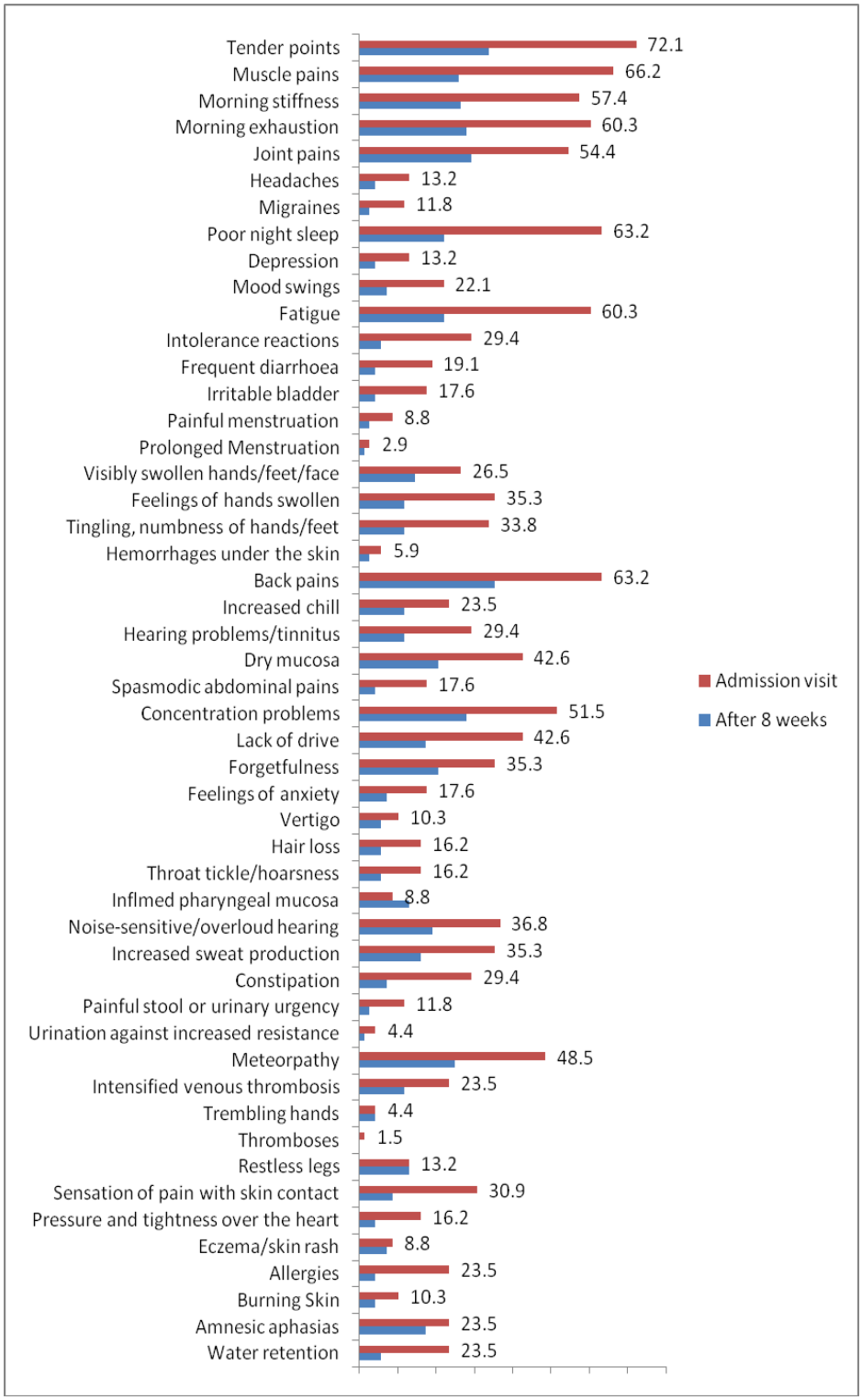
Indicted is the expressivity of the respective symptom 8 weeks after start of treatment. The percentages always relate to all 68 patients. On account of the missing details (above all with questions regarding menstruation), the addition of patient details does not always result in 100%




Graphic 7

### 3.3.5. Severe expressivity of symptoms during initia l& final documentation

Percentage representation of the respective very severe symptoms during initial & final documentation:




Graphic 8

## 3.4. Improvement rates

During the control documentations held after 2, 4, 6 and 8 weeks, the expressivity of all symptoms with most patients was much lower that at the start of treatment. For instance, the symptoms ‘migraines’ had improved with 86.2% and ‘intolerance reactions’ with 80.4% of the concerned patients. Amongst other things, further very high improvement rates were established for the symptoms ‘painful stool or urinary urgency’ (78.9%), ‘irritable bladder’ (73.7%), ‘spasmodic abdominal pains’ (72.7%), ‘constipation’ (72.5%), ‘burning skin’ (71.7%) and ‘allergies’ (70.8%). The expressivity of tender points had improved by at least 50% of the concerned patients.

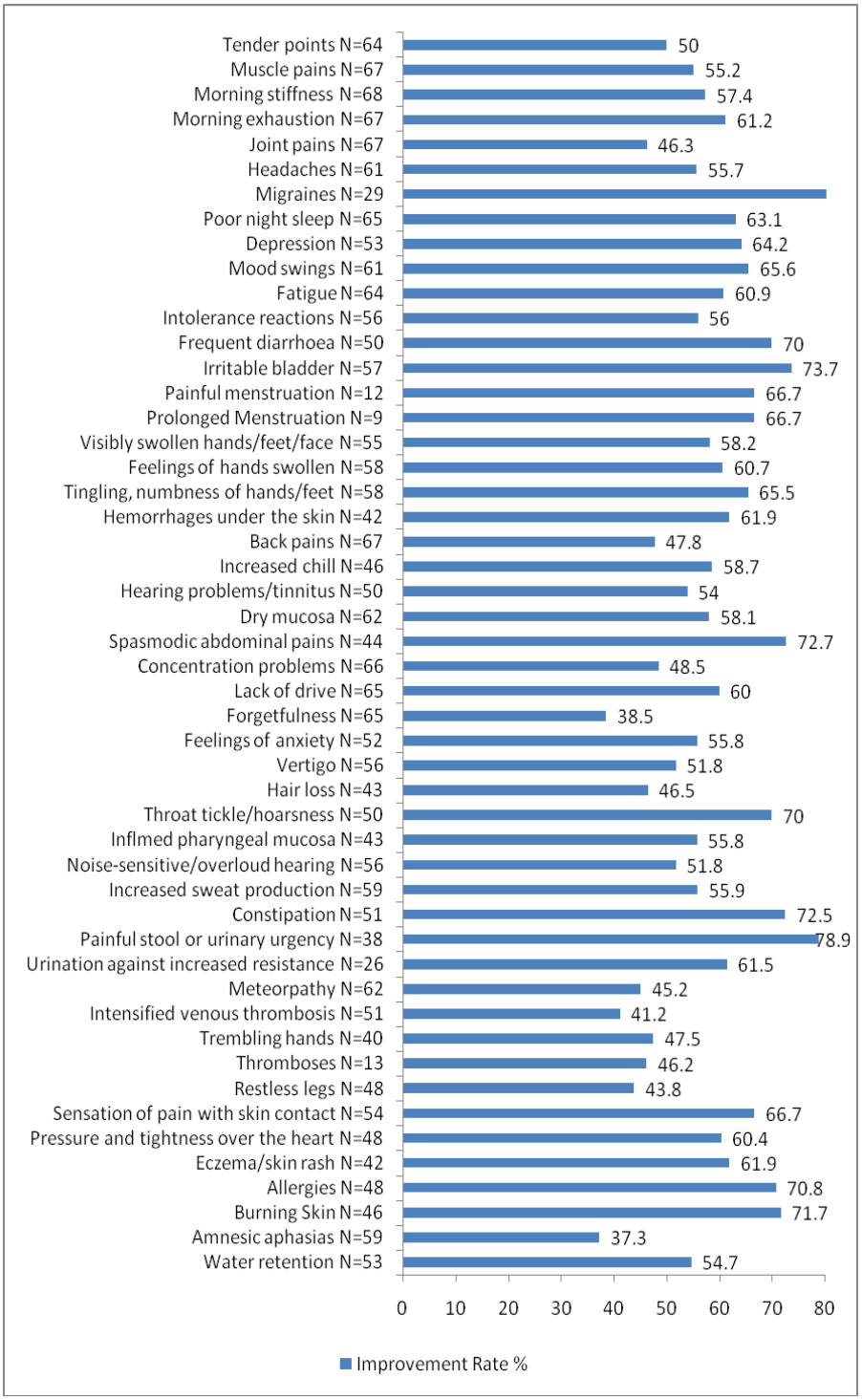
With 63.2% of patients, the general state of health after an 8-week dietary change had improved in comparison to the admission visit, whereas the general state of health remained unchanged amongst 29.4% and it had deteriorated amongst 7.4%.

The presented results have been graphically depicted in the form of improvement data for better overview.

In this connection it is to be noted that only those patients have been included in which the respective symptom was at least ‘less expressive’ in at least one point in time. Patients with which the respective symptom was not expressive at all documentation points were therefore not utilized for Graphic 9.

### 3.4.1. Improvement rates of symptoms

Depicted is the percentage of patients in which the expressivities of the respective symptoms have improved in the observation period. Patients in which the symptom was neither expressive at the start of treatment nor during the last documentation after 8 weeks have not been taken into account.




Graphic 9

### 3.4.2. Exemplary symptom scores in the course

In order to exemplarily illustrate the development of symptoms in the course of the observation period, the symptom scores (mean values calculated from 0=nonexistent, 1=less, 2=moderate and 3=very severe) have been calculated for some symptoms for each documentation point and graphically depicted. In this connection it is to be noted that only those patients have been included in which the respective symptom was at least 'less expressive' in at least one point in time. Patients with which the respective symptom was not expressive at all documentation points were therefore not utilized for the following tables and illustrations.

Only patients with which the symptom was expressive in at least one point in time; mean values calculated from 0=nonexistent, 1=less, 2=moderate, 3=severe

| **Development of symptom "tender points"** | **Mean Value** | **Standard Deviation** | **Median** | **Number** |
|---|---|---|---|---|
| Start | 2.69 | 0.61 | 3.0 | 64 |
| After 2 weeks | 2.34 | 0.74 | 2.0 | 64 |
| After 4 weeks | 2.16 | 0.86 | 2.0 | 64 |
| After 6 weeks | 2.08 | 0.82 | 2.0 | 64 |
| After 8 weeks | 2.06 | 0.83 | 2.0 | 34 |

Table 18

| **Development of symptom "migraines"** | **Mean Value** | **Standard Deviation** | **Median** | **Number** |
|---|---|---|---|---|
| Start | 1.90 | 0.80 | 2.0 | 30 |
| After 2 weeks | 1.17 | 1.12 | 1.0 | 30 |
| After 4 weeks | 1.07 | 1.11 | 1.0 | 30 |
| After 6 weeks | 0.71 | 0.85 | 0.5 | 30 |
| After 8 weeks | 0.66 | 0.94 | 0.0 | 30 |

Table 19

| **Development of symptom "poor night sleep"** | **Mean Value** | **Standard Deviation** | **Median** | **Number** |
|---|---|---|---|---|
| Start | 2.53 | 0.71 | 3.0 | 66 |
| After 2 weeks | 2.09 | 0.78 | 2.0 | 66 |
| After 4 weeks | 1.97 | 0.78 | 2.0 | 66 |
| After 6 weeks | 1.86 | 0.92 | 2.0 | 66 |
| After 8 weeks | 1.68 | 0.94 | 2.0 | 66 |

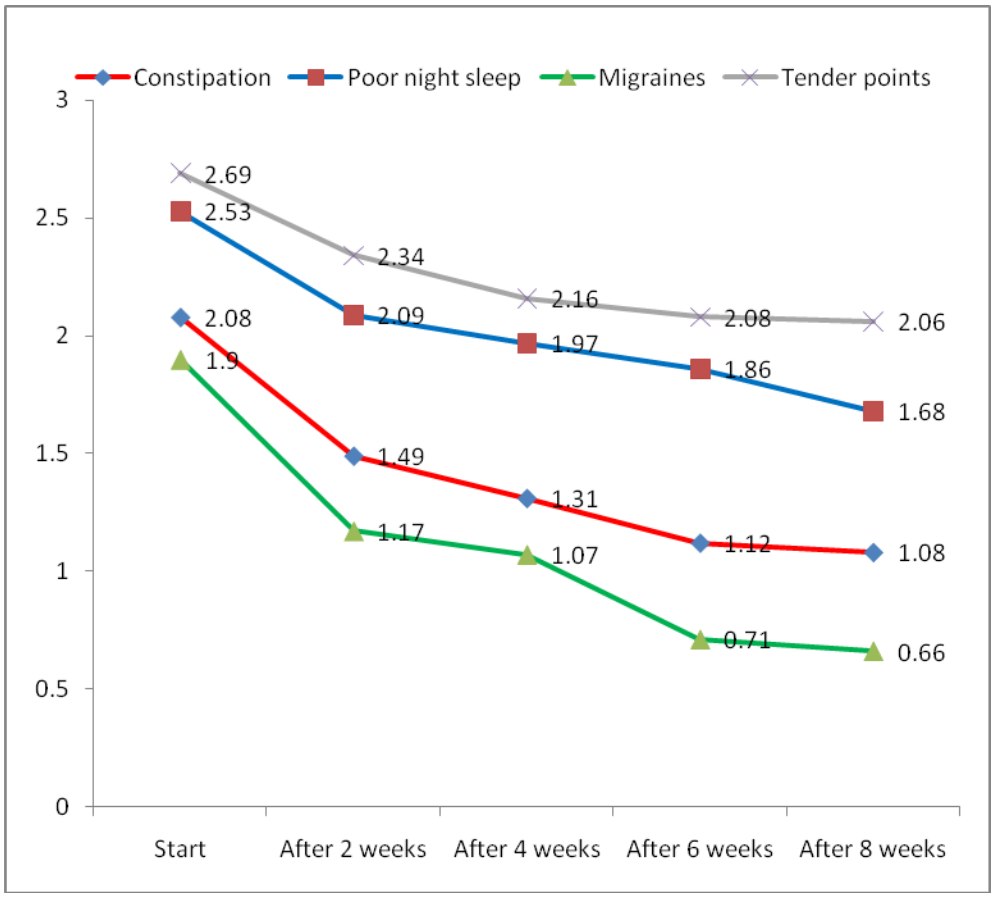
Table 20

| Development of symptom "constipation" | Mean Value | Standard Deviation | Median | Number |
|---|---|---|---|---|
| Start | 2.08 | 0.87 | 2.0 | 51 |
| After 2 weeks | 1.49 | 1.10 | 2.0 | 51 |
| After 4 weeks | 1.31 | 1.12 | 1.0 | 51 |
| After 6 weeks | 1.12 | 1.02 | 1.0 | 51 |
| After 8 weeks | 1.08 | 0.96 | 1.0 | 51 |

Table 21

**Development of some symptom scores**

Depiction of symptom scores (mean values calculated from 0=nonexistent, 1=less, 2=moderate and 3=very severe) for 4 exemplary symptoms in the course. In this connection it is to be noted that only those patients have been included in which the respective symptom was expressive in at least one point in time.




Graphic 10

## 3.5. Consistency during the dietary change in the course (compliance)

In addition to development of symptoms, questions regarding the experiences gained within the framework of dietary change should be documented: about two thirds of the 68 patients assessed their consistency during the dietary change after 2 weeks with ‘very good’ or ‘good’. The percentage of these patients remained constant after 4 weeks, then sagged after 6 weeks to under 60%, and then increased again to 63% up until the end after 8 weeks.

The percentage of patients which assessed their consistence as ‘poor’ or ‘very poor’ amounted to 10% in the beginning.

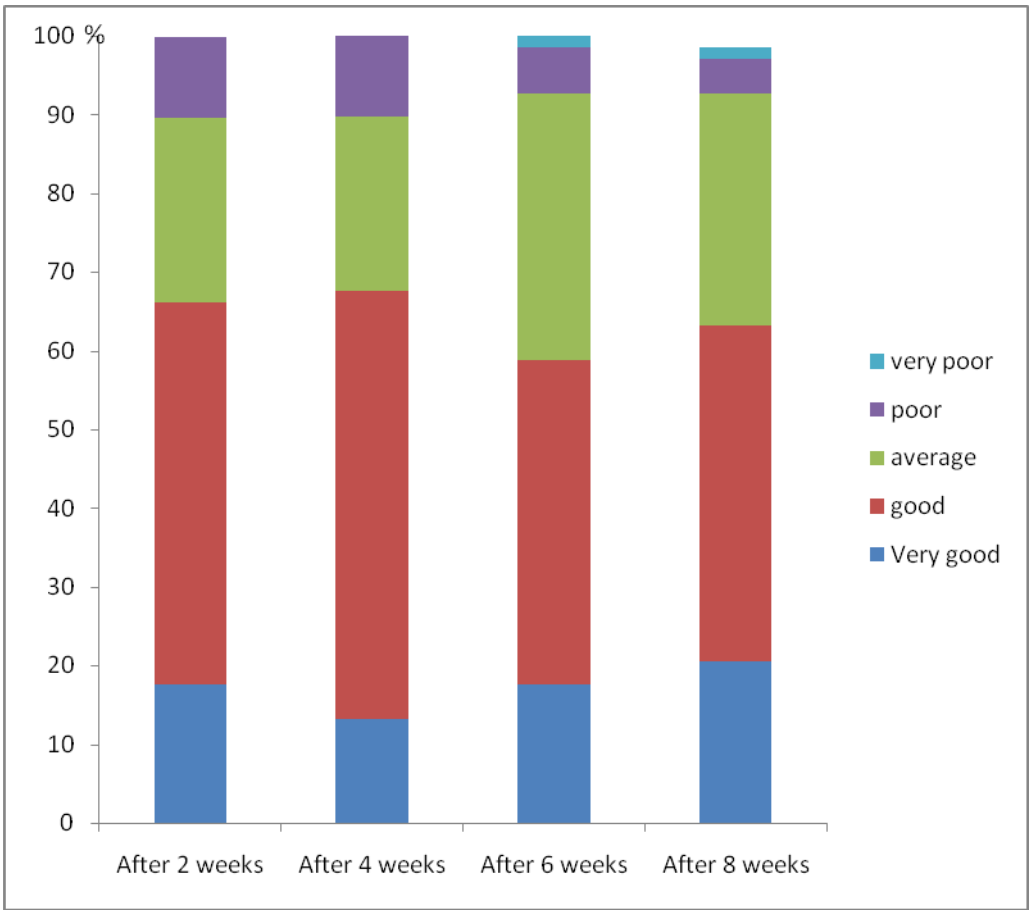
Two weeks after start of treatment, 42.6% of all patients documented that the immunologically-adapted dietary change was ‘difficult’ or ‘very difficult’ for them. After 4 weeks, only 27.9% of all patients indicated that the retention of new eating habits was ‘difficult’ or ‘very difficult’ for them. The percentage of these patients decreased after 6 weeks to 22.1%, and at the end of the observation period after 8 weeks amounted to 26.5%.

### 3.5.1. Consistency of dietary change in the course

**How difficult is it today for you to retain your new eating habits?**

| Consistency during the dietary change | | | | |
|---|---|---|---|---|
| | **After 2 weeks** | **After 4 weeks** | **After 6 weeks** | **After 8 weeks** |
| Very good | 17.6 % | 13.2 % | 17.6 % | 20.6 % |
| Good | 48.5 % | 54.4 % | 41.2 % | 42.6 % |
| Average | 23.5 % | 22.1 % | 33.8 % | 29.4 % |
| Poor | 10.3 % | 10.3 % | 5.9 % | 4.4 % |
| Very poor | 0 % | 0 % | 1.5 % | 1.5 % |
| No data | 0 % | 0 % | 0 % | 1.5 % |
| Total | 100.0 % | 100.0 % | 100.0 % | 100. 0 % |

Table 22




Graphic 11

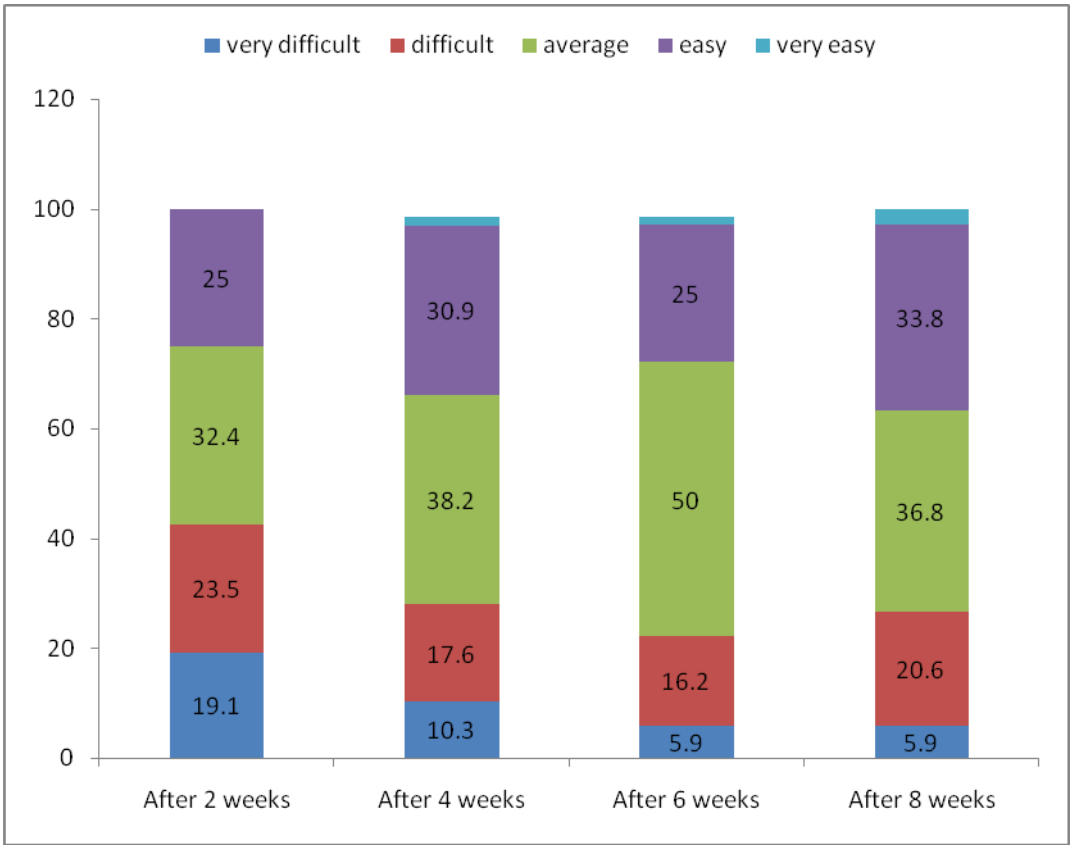
### 3.5.2. Retention of new eating habits

Two weeks after start of treatment, 42.6% of all patients documented that the dietary change was ‘difficult’ or ‘very difficult’ for them. After 4 weeks, only 27.9% of all patients indicated that the retention of new eating habits was ‘difficult’ or ‘very difficult’ for them. The percentage of these patients decreased after 6 weeks to 22.1%, and at the end of the observation period after 8 weeks amounted to 26.5%.

**Assessment for the last respective period up until the current documentation**

| **Retention of eating habits** | | | | |
|---|---|---|---|---|
| | **After 2 weeks** | **After 4 weeks** | **After 6 weeks** | **After 8 weeks** |
| Very good | 19.1 % | 10.3 % | 5.9 % | 5.9 % |
| Good | 23.5 % | 17.6 % | 16.2 % | 20.6 % |
| Average | 32.4 % | 38.2 % | 50.0 % | 36.8 % |
| Poor | 25.0 % | 30.9 % | 25.0 % | 33.8 % |
| Very poor | 0 % | 1.5 % | 1.5 % | 2.9 % |
| No data | 0 % | 1.5 % | 1.5 % | 1.5 % |
| Total | 100.0 % | 100.0 % | 100.0 % | 100. 0 % |

Table 23




Graphic 12

## 3.6. Weight change in the course

In the course of the approximate 8-week dietary change, a weight decrease could be document in 86.8% of all patients. The average weight of patients at the start of treatment amounted to 78.5 kg, and continuously decreased via 77 kg (after 2 weeks), 76.0 kg (after 4 weeks) and 75.2 kg (after 6 weeks) to 74.9 kg. The mean value of weight loss amounted to 3.6 kg (maximum: 10.9 kg). If one considers the relative weight change in comparison to the initial weight, it turned out that the patients had lost 4.9% of their body weight on average in the course of the 8-week observation period. The maximum weight loss amounted to 15% of body weight.

### 3.6.1. Weight after 8 weeks in comparison with initial weight

| | Sex | | | | Total | |
|---|---|---|---|---|---|---|
| | Male | | Female | | | |
| Age (years) | Number | % | Number | % | Number | % |
| Higher | 0 | 0 % | 4 | 6.7 % | 4 | 5.9 % |
| Unchanged | 0 | 0 % | 5 | 8.3 % | 5 | 7.4 % |
| Lower | 8 | 100.0 % | 51 | 85.0 % | 59 | 86.8 % |
| **Total** | **8** | **100.0 %** | **60** | **100.0 %** | **68** | **100.0 %** |

Table 24

### 3.6.2. Absolute weight change after 8 weeks in comparison with initial weight

| Weight change after 8 weeks [kg] | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Sex | Mean Value | Standard Deviation | Min. weight loss | Max. weight loss | Percentile | Median | Percentile | Valid N |
| Male | -4.9 | 2.3 | -7.8 | -1.0 | -6.9 | -5.3 | -3.2 | N=8 |
| Female | -3.4 | 2.8 | -10.9 | 1.5 | -5.3 | -3.2 | -1.1 | N=60 |
| Total | -3.6 | 2.7 | -10.9 | 1.5 | -5.7 | -3.5 | -1.4 | N=68 |

Table 25

### 3.6.3. Relative weight change after 8 weeks

Solely the absolute weight changes have only a limited expressivity. The consideration of relative weight change in comparison with initial weight is more helpful here.

On average, the patients lost 4.9% of their body weight (median: 4.7%) in the course of the 8-week observation period. The maximum weight loss amounted to 15% of body weight.

**Weight change percentage after approx. 8 weeks in comparison with initial weight**

| Sex | Mean Value | Standard Deviation | Min. weight loss | Max. weight loss | Percentile | Median | Percentile | Valid N |
|---|---|---|---|---|---|---|---|---|
| Male | -6.5 | 3.7 | -14.4 | -1.3 | -7.6 | -5.9 | -5.1 | N=8 |
| Female | -4.7 | 3.9 | -15.0 | 2.1 | -7.2 | -4.2 | -1.5 | N=60 |
| Total | -4.9 | 3.9 | -15.0 | 2.1 | -7.2 | -4.7 | -2.1 | N=68 |

Table 26

### 3.6.4. Development of body weight in the observation period

The weight should be documented at the start of treatment as well as during the controls after 2, 4, 6 and 8 weeks. The following table lists the mean values of weight details along with standard deviation and median for all documentation points. A graphic illustrates the development.

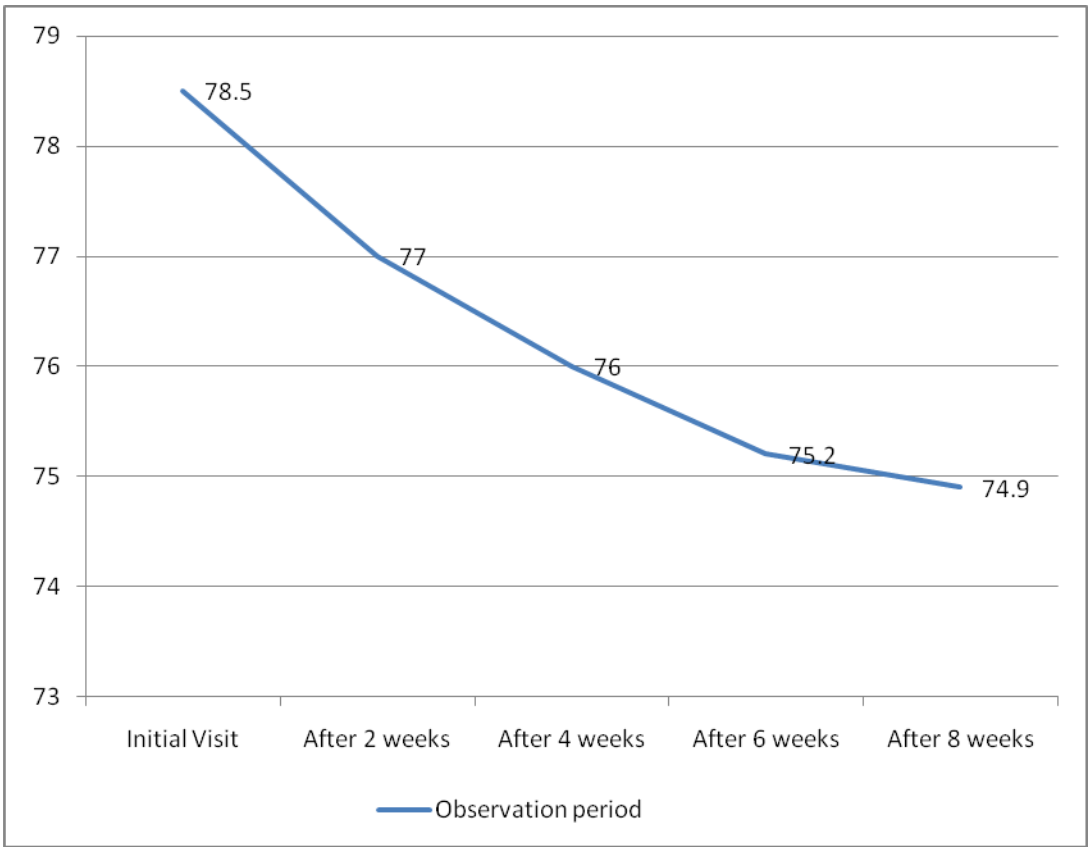
**Development of body weight [kg]**

| | Mean Value | Standard Deviation | Median | Valid N |
|---|---|---|---|---|
| Initial visit | 78.5 | 16.8 | 76.3 | N=68 |
| After 2 weeks | 77.0 | 16.6 | 74.2 | N=68 |
| After 4 weeks | 76.0 | 16.5 | 73.0 | N=68 |
| After 6 weeks | 75.2 | 16.6 | 72.0 | N=68 |
| After 8 weeks | 74.9 | 16.3 | 72.0 | N=68 |

Table 27

### 3.6.4.1. Weight development in the course

The mean value of body weight at the respective documentation point is always depicted.




Graphic 13

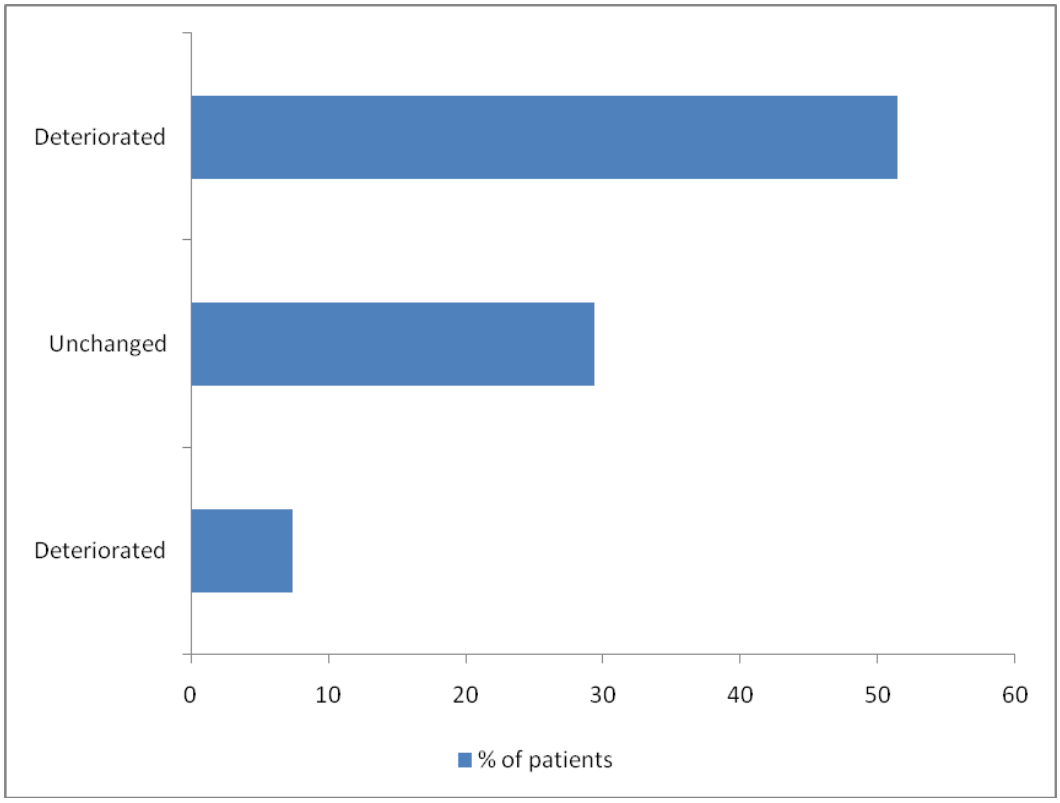
## 3.7. Change of general state of health

With 63.2% of patients, the general state of health after an 8-week dietary change had improved in comparison to the admission visit, whereas the general state of health remained unchanged amongst 29.4% and it had deteriorated amongst 7.4%.

**Change of general state of health after 8 weeks**

| | Sex | | | | Total | |
|---|---|---|---|---|---|---|
| | Male | | Female | | | |
| **Health** | **Number** | **%** | **Number** | **%** | **Number** | **%** |
| Improved | 4 | 50.0 % | 39 | 65.0 % | 43 | 63.2 % |
| Unchanged | 3 | 37.5 % | 17 | 28.3 % | 20 | 29.7 % |
| Deteriorated | 1 | 12.5 % | 4 | 6.7 % | 5 | 7.4 % |
| **Total** | **8** | **100.0 %** | **60** | **100.0 %** | **68** | **100.0 %** |

Table 28




Graphic 14

## 3.8. Further changes

In addition to the predetermined symptoms, so-called ‘further changes’ (between 1 and 9 mentions, 161 mentions altogether) had been indicated as clear texts with 63 patients. These statements were coded and summarized in groups.
Most frequently mentioned were ‘weight loss’ (69.1% of patients), followed by ‘fitter’ (38.2% of patients), ‘more seldom tired’ (36.8%) and ‘better skin’ (26.5%).

**Further changes**

| Changes | Number | % |
|---|---|---|
| Better skin | 18 | 26.5 |
| Fitter | 26 | 38.2 |
| More seldom tired | 25 | 36.8 |
| Gastrointestinal complaints improved/gone | 13 | 19.1 |
| Weight loss | 47 | 69.1 |
| Happier, livelier, more balanced | 8 | 11.8 |
| Negative observations | 10 | 14.7 |
| Positive observations (other) | 14 | 20.6 |

Table 29

## 3.9. Final assessment of efficacy

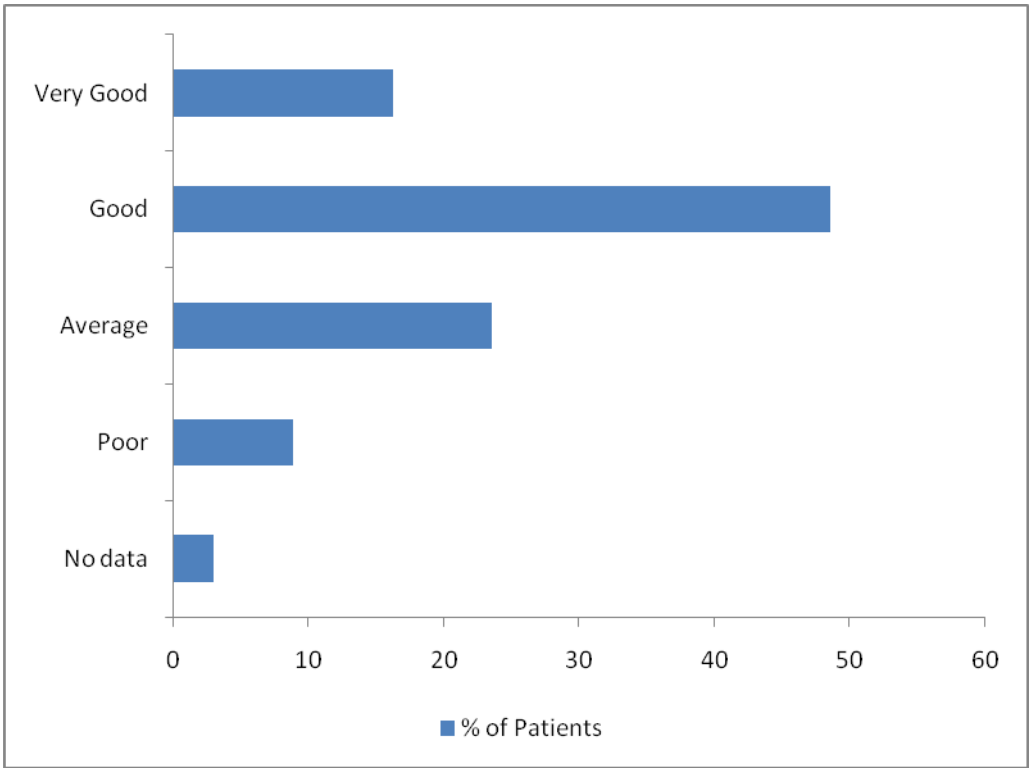
Nearly two thirds of the patients (64.7%) assessed the efficacy of dietary change with ‘very good’ or ‘good’, and altogether 82.4% of all patients would recommend this therapeutic approach.

**Patient opinion of efficacy**

| | Sex | | | | Total | |
|---|---|---|---|---|---|---|
| | Male | | Female | | | |
| **Efficacy** | **Number** | **%** | **Number** | **%** | **Number** | **%** |
| Very good | 2 | 0 % | 11 | 18.3 % | 11 | 16.2 % |
| Good | 6 | 75.0 % | 27 | 45.0 % | 33 | 48.5 % |
| Average | 1 | 12.5 % | 15 | 25.0 % | 16 | 23.5 % |
| Poor | 1 | 12.5 % | 5 | 8.3 % | 6 | 8.8 % |
| No data | 0 | 0.0 % | 2 | 3.3 % | 2 | 2.9 % |
| **Total** | **8** | **100.0 %** | **60** | **100.0 %** | **68** | **100.0 %** |

Table 30

**Final patient assessment of efficacy**




Graphic 15

### 3.9.1. Recommendation

Altogether 82.4% of all patients would recommend the diagnostics and therapy.

| | Sex | | | | Total | |
|---|---|---|---|---|---|---|
| | Male | | Female | | | |
| **Recommendation** | **Number** | **%** | **Number** | **%** | **Number** | **%** |
| Yes | 6 | 75.0 % | 50 | 83.3 % | 56 | 82.4 % |
| No | 1 | 12.5 % | 7 | 11.7 % | 8 | 45.8 % |
| None | 1 | 12.5 % | 3 | 5.0 % | 4 | 5.9 % |
| **Total** | **8** | **100.0 %** | **60** | **100.0 %** | **68** | **100.0 %** |

Table 31

# 4. Discussion

The fibromyalgia syndrome presents a vast number of complaints and symptoms. Establishing a diagnosis is more difficult as a result. The pathogenesis of the illness has not been clearly clarified up to now. In addition to the classic medicamentous therapies with analgesics, muscle relaxants or antidepressants, there are a vast number of therapeutic approaches. Fibromyalgia patients deal with increase of complaints with alternative medical therapeutic procedures [58,59]. They equally seem to benefit from the application of these procedures [60].

One of the most frequent approaches in alternative medicine is the application of dietetic measures. The number of patients who attempt a diet (omission attempt or supplementation with foodstuffs or additives) is indicated with 26-40% [59,61]. Similar numbers are found in related illnesses such as chronic fatigue syndrome. In this case, 54% of patients indicated having attempted a diet. Of these patients, 74% were of the opinion that the diet attempt improved their illness [62]. It is evident that dietetic measures are subjectively and objectively helpful in the treatment of fibromyalgia [63,64,65,26,27,53].

The connection between allergic-inflammatory reactions of type III allergy to food and the frequent complaints with regard to fibromyalgia should be clarified with the paper at hand. This immunological approach in the diagnostics and therapy of fibromyalgia was not the emphasis of research in the previously known papers. Moreover, food allergies are frequently reduced to the type I allergy. The necessary IgG diagnostics are often not undertaken as a result.

The diagnosis of a food allergy requires a careful anamnesis and thorough clinical examination. The examination by means of prick test and RAST usually detects IgE antibodies. Since a number of allergies are not IgE mediated, we must inevitably reckon with erroneous negative findings. For instance, patients who react quickly to cow's milk protein frequently have positive prick test results, whereas the delayed reacting patients do not react [30]. There is a slight correlation between food provocation test and prick test [7,34]. Mast cells of the gastrointestinal tract (GIT) differ from mast cells of the connective tissue with regard to their characteristics, amongst other things also with regard to their mediator substances of intracellular granules and the stimuli which leads to their release. Therefore a positive cutaneous reaction does not have to be synonymous with a positive reaction in the GIT [4,29,40,47,]. RAST

and ELISA track down antibodies against food. A correlation between the laboratory result and the clinical findings could not always be established. For instance, IgE and IgG antibodies against food are also found in complaint-free patients [5,47]. This prompted the authors to postulate that this is an indication for the irrelevance of an IgG and IgE diagnosis. One could assume that the existence of IgG in asymptomatic individuals could be an indication that the organism always produces IgG on the presentation of a foodstuff over the course of time. It is to be countered that patients with a completely unbalanced diet also do not show any increased IgG level in a great number. Possibly the symptom-free patients with increased IgG levels at the time of examination simply have better compensation possibilities. Papers regarding celiac disease were able to show that there are asymptomatic gene carriers which can never – or only after years – develop complaints [36,52].

At the same time, the long-term exposition seems to have a certain significance vis-à-vis the potential allergen [1,12]. In my opinion, this is also an indication of an up to now functioning compensation mechanism. Tolerance now becomes intolerance.

The connection between allergy and fibromyalgia or generally the complaints of patients is ideally verifiable through a placebo-controlled, double-blind study. This is possible in special cases. However, this approach is not ordinarily suitable in practical reality. The understandable desire to conduct a double-blind, placebo-controlled study in order to diagnose IgG-mediated food allergies and to implement a subsequent elimination diet encounters limits. David demonstrates these as follows:

Limits and difficulties of a double-blind, placebo-controlled study according to David [16]:

- Unclear dose-effect relationship
- Difficulties with concealing some substances
- Altered means of intake
- Difficulties taking a capsule
- Danger of anaphylaxis
- Additive effects of various foodstuffs

A double-blind, placebo-controlled study is thus an impracticable way to answer questions posed in this study.

Simpler testing methods which determine the incompatible foodstuff with greater precision are therefore required. At the same time, false positive reactions can be more accepted than false negative findings. A single false negative finding with one

basic foodstuff can call the effectiveness of measures into question. In allergological practice, with the type I allergy one generally relies on the detection of specific IgE. An oral provocation is reserved for severe or unclear cases. Up to now, no great importance has been attached to the detection of specific IgG. This is incomprehensible, since particularly IgG is recognized in the mediation of inflammatory reactions with infectious diseases. The role of the IgG antibody in the treatment of celiac disease is already established [67]. So it is astonishing that in August 2002 a review was published in *The Lancet* in which only the IgE-mediated food allergy is causally mentioned under the heading “food allergy”, whereas all other reactions are subsumed as food intolerances [68].

The importance of IgG antibody in the pathogenesis of allergic-inflammatory illnesses is negated by several authors. They understand the formation of IgG as a normal reaction of the body to the supplied nutritional allergens [69,70,71,72]. However, studies on atopic children show that in contrast to healthy children, these children form lastingly high IgG (and IgE) titer against milk and chicken protein [73,74]. This corroborates a fundamental immunological disorder with involvement of IgG. This hypothesis is supported through proven increased IgG titer with respiratory allergies. So it has to be postulated that the immunological hypersensitivity (allergy) to food knows more than one reaction pathway. In intraindividual terms, this can dominate IgG or IgE formation.

The paper at hand shows that particularly with the fibromyalgia syndrome, the detection of specific IgG against foodstuff and an elimination diet building on this has a high success rate in the therapy.

These successes first of all pertain to the general state of health of the respondents. For instance, at least 63.2 % of all study participants indicate an improvement of the general state of health in this connection. Women (65%) seem to benefit more strongly than men (50%). The positive overall result through the very high percentage of the recommendations of the diagnostic and therapeutic approach undertaken in the work is emphasized. At least 82.4% are willing to recommend this procedure. Therefore it is clear that in addition to the amelioration of complaints, an additional benefit has emerged for the study participants as a result of the applied elimination diet.

All classic complaints of fibromyalgia can be significantly improved through an IgG-

adapted elimination diet during the treatment of individual symptoms. For instance, the tender points reduce amongst 50% of the patients, muscle pains amongst 55.2 %, morning feeling of exhaustion amongst 61.2%, sensation of pain with skin contact amongst 66.7%, burning skin amongst 71.7% and morning stiffness amongst 57.4%. Particularly high improvement rates are found with migraine-like headaches (86.2%), emotional complaints such as depressions (64.2%), mood swings (65.6%), poor sleep (63.1%) and fatigue (60.9%). Above-average improvement rates are also found with gastrointestinal symptoms such as painful stool or urinary urgency (78.9%), spasmodic abdominal pains (72.7%) and constipation (72.5%).

The submitted paper thus shows that in addition to a general improvement, the manifold pain syndromes and the emotional well-being of patients will also be improved through an elimination diet if this diet avoids foodstuffs in which an increased specific IgG level has been measured. This allows the conclusion that the type III allergy plays a noteworthy role in the development or at least with regard to the severity of fibromyalgia complaints.

A prerequisite for the expressivity of a food allergy is possibly that foodstuffs penetrate the intestine and will then be recognized as exogenous. A healthy intestine is lined by a mucous membrane, a strong, particularly stably structured defense system. The first pathogens are already repelled here. Another function of the intestine is the extensive separation of nourishment into component parts so that they can be absorbed in the blood. From there they reach the body cells, where they fulfill numerous tasks. Infections, stress, medicaments such as antibiotics and antiphlogistic agents as well as a disturbed intestinal flora destroy this equilibrium and bring about an increased permeability of the small intestine, whereby larger undigested or not completely digested nutritive elements can penetrate the blood. A permanently increased intestinal permeability leads to a continual increase of food intolerances — measurable with the concomitance of increased IgG antibodies against this foodstuff [10,29,45,51].

## Medical importance of IgG antibodies against food

If IgG antibodies against food can be detected, this is a very reliable sign that constant contact between food and the immune system comes about. It could be proven that the concentrations of antibodies diminish and finally vanish if the corresponding foodstuffs will be avoided for a while.

The antibody binds to the foodstuff and an immune complex emerges. This activates the complement system – a part of the immune cascade – and thus attracts phagocytes (“scavenger cells” which “digest” the intruders and thus make them innocuous), which destroy the immune complex. At the same time, various signal substances of the immune system (interleukin, TNF-$\alpha$) will release large quantities of oxygen radicals (O $\bullet$) and proteases.

TNF-$\alpha$ has a predominantly phlogistic effect in the tissue, where it is formed in the course of immune response. Oxygen radicals can also attack and destroy endogenous cells. This happens with a surplus of oxygen radicals if in the absence of antioxidants the endogenous cells are no longer able to protect themselves against an oxidation (decomposition of the cell membrane’s components) through the oxygen radicals. Moreover, oxygen radicals can decompose (oxidize) the cell fatty substances (lipids) which normally keep the cell membranes smooth, with the result of cell destruction. Proteases are enzymes which decompose unspecific proteins and can thus also destroy surrounding body tissue. If the immune complexes are found in lesser number, this occurs without appreciable damages. On the other hand, in the event of intolerance, the immune complexes are available in a larger concentration. These affix to certain activated cells of the blood vessels, can leave the bloodstream and settle in the tissue. Immune complexes repeatedly settle on these activated cells and lead to chronic local inflammations. These are responsible for a vast number of chronic complaints. Since these inflammatory processes continually proceed, more and more mediators will be formed, which subsequently interfere in numerous metabolic processes such as with insulin resistance.

## Why is the importance of food intolerance only recognized now?

Food intolerances give rise to varying symptoms. They partially resemble the symptoms of an allergy. As a result, they have often been erroneously designated as food allergy, although the markers responsible for this are not detectable. The time delay between ingestion and onset of symptoms makes detection difficult. Astonishingly, the author was able to find very few scientific papers which address the connection between food and myalgias or rheumatic illnesses [15,18,25,27,28,37,53,55]. A connection between complaints and nutritional habits is evident. An immunological / allergological approach is thereby the exception. Hafstrom et al. [25] show a connection between gluten-free nutrition and rheumatoid arthritis. In accordance with the notion that especially with a type III allergy increased immune complexes form and these can be deposited in soft parts and joints, the subsequent inflammatory reaction explains the complaints of these patients. Myalgic complaints are generally known within the framework of IgE-mediated allergies, yet the type III allergy is particularly predisposed towards inflammatory reactions.

Enestrom et al. frequently found deposits of mast cells as well as IgG intradermal and in the vascular walls with fibromyalgia patients, and thus allow the hypothesis of a neurogenic inflammation [19,20]. In 1998, Baraniuk et al. found markers of an increased vascular permeability and augmented IgG secretion in the nasal secretion, but precluded a causal connection because there was also one group of affected patients which did not these markers [2]. But possibly this is to be assessed more as an indication of a multicausal phenomenon, since the results presented here point out that there is a connection between the complaints of fibromyalgia and the existence of specific IgG. At the same time, it cannot be said with certainty whether the type III allergy is the cause or whether it acts as an additional trigger. For the clinical practice, IgG diagnostics against specific foodstuffs offer a valuable approach for gaining substantial relief for the patients.

In the opinion of the author, it is erroneous if the IgE determination or a prick test will be utilized as a screening instrument in the consideration of food allergies, yet a specific IgG diagnosis is not undertaken. The results of this paper clearly show that there is a connection between increased IgG levels and complaints. Amongst other things, a repeated attack by free radicals leads to a further chronification, further damages in the long term, and possibly accelerates the progress of such illnesses as a result of the inflammatory activity situation which is more pronounced vis-à-vis the type I allergy.

It is already customary to determine IgG antibodies – e.g. against gluten with celiac disease – with individual diseases [38]. However, even an individual analysis is very expensive. But this rarely concerns monocausal sequences in which only one allergen is involved. The vast number of basic foodstuffs used in everyday life necessitates broad screening. For one thing, it is a matter of identifying the potential allergens in order to prevent the allergic-inflammatory events. For the clinical daily routine it is furthermore decisive to give the patients a recommendation regarding what they can eat. In my opinion, a broadly applied diagnosis is not only useful with regard to the aspiration of a diversified diet, it is virtually a prerequisite for a successful therapy. A diversified diet is also the basis for avoiding malnutrition.

In the past, the relatively high costs arising in this connection have certainly contributed towards refraining from this examination. Or dietary recommendations based on the testing of 10 or 15 foodstuffs were implemented. This usually did not render the desired success, since the recommendations also allowed incompatible foodstuffs which were not tested. On the other hand, fasting cures – the most stringent form of omission diet – are often successful, since all incompatible foodstuffs will also be automatically avoided.

If one considers that an undetected type III food allergy accelerates the progress of a chronic illness or leads to a deterioration of symptoms, follow-up costs will be caused because of this, which are not in any proportion to the financial expenditure of a specific IgG diagnosis.

The utilization of orthomolecular substances – such as vitamins, minerals, fatty acids, etc. – with chronic inflammatory illnesses and the reduction of free radicals is being increasingly discussed. With a dietary change as described here, the causal emergence of free radicals can be diminished. The basic inflammatory events will be reduced as a result. The study at hand was able to show that quite a few complaints improved under an elimination diet. This possibly results from the reduction of free radicals and inflammatory mediators.

### Why conduct a test of all IgG subclasses?

There are the following varying systems which are utilized for detection of food intolerance.

**$IgG_4$ test:** detects only $IgG_4$ antibodies; the test is unsuitable for diagnosing an incompatibility in infants, since $IgG_4$ is not transmitted on a transplacental basis.

**ANT:** is a nutrophil function test. The difference of neutrophils in the quiescent state and after exposure with foodstuffs is measured. Only antibodies which have opsonizing characteristics (i.e. antibodies of class $IgG_1$ and $IgG_3$) will be detected.

A great disadvantage of the method is that reproducible results are only to be anticipated with fresh blood or serum. Furthermore, disturbances can emerge upon existence of infections or through any existing antiphlogistic medicaments. Therefore it is only usable on a limited basis.

The granulocytic transformation tests do not detect any $IgG_4$, since this has insufficient opsonizing capacities. But in order to cover $Th_1$ as well as $Th_2$ reactions, all subtypes are necessary. Reproducible results are also only achievable here with fresh blood.

| **Activity** | **$IgG_1$** | **$IgG_2$** | **$IgG_3$** | **$IgG_4$** |
|---|---|---|---|---|
| Neutralization | ++ | ++ | ++ | ++ |
| Opsonization | +++ | * | ++ | (+) |
| Sensitization of mast calls | + | - | + | - |
| Complement activation | ++ | + | +++ | (+) |
| Transport through the placenta | +++ | + | ++ | (+/-) |
| Extravascular diffusion | +++ | +++ | +++ | +++ |
| $Th_1$ - $Th_2$ | $Th_2$ | $Th_1$ | $Th_1$ + $Th_2$ | $Th_2$ |
| reaction type | Type 2 | Type 4 | Type 3 | Type 1 |
| mean concentration | 9 | 3 | 1 | 0.5 |

Table 32

Only a test that records all characteristics of the IgG classes is able to actually depict all forms of intolerance and the related immunological reaction.

IgG antibodies are components of acquired, adaptive immunity. They bind to the specific antigen for them and thus initiate the immunological reaction for destruction of the antigen. While doing so, they act as an opsonin and make the antigen visible for the scavenger cells. The complement system is also activated, which attracts the phagocytes. They have a high persistence and are detectable in the serum.

This makes them popular markers in infection serology for any infection that has occurred. However, one cannot differentiate whether it was a longstanding contact or a recent contact. Since they bind the antigens and release for destruction, and thus prevent that these antigens propagate in the body, protective characteristics are attributed to them and apply as a standard for the immunity against a specific germ.

The behavior is similar, yet different, with foodstuffs. Since foodstuff cannot propagate in the body, the supposed protective factor does not play any role. Although one encounters an infectious antigen such as a hepatitis virus yet quite seldom, we still eat the same things every day, such as bread or milk products. If there is an incompatibility, the bread or milk antigens will be combated in the same way as the virus antigens, with the result of a chronic inflammation. The supposed protective characteristic of the IgG antibody has now turned out to be a rather burdening characteristic.

Within the framework of an elimination diet there are a series of variables which cannot always be precisely recorded, and the results can vary. These variables are depicted as follows:

**Reasons for an unsatisfactory result of an elimination diet according to David [16]:**

- The test person is not allergic to the foodstuff.
- The omission period was too short.
- The foodstuff was incompletely avoided (hidden ingredients, etc.).
- The test person is allergic to other non-tested foodstuff.
- The test person had an intercurrent illness.
- The symptoms were inordinately indicated.

But during weighting of these variables, these mainly lead to a poorer result. So the results achieved here can possibly be improved even more if it is possible to control individual variables more precisely. However, an omission period that is too short or undetected (hidden) incompatible foodstuffs can worsen the result. The cooperation between patient and physician during anamnesis and therapy is a decisive factor for success.

If one compares the results of the paper at hand with other works which have examined medicamentous therapeutic approaches, they will discover that the IgG-adapted elimination diet provides at least equally good results. For instance, the general state of health (as status “overall”) improved by 63.2% within the observation period of 8 weeks. In particular, migraines and the gastrointestinal symptoms of the fibromyalgia patients even had much greater improvement rates (up to 86%). In subjective terms, the benefit of such a dietary change was recognized by 84.2%, which can be realized in the degree of recommendation.

The benefit of medicamentous therapy is indicated for amitriptyline with 74%, for moclobemide with 54% and 49% with placebo [75]. However, undesirable effects with this medication are also found with amitriptyline (77%) and with moclobemide (74%) [75]. Combinations such as tramadol/acetaminophen also do not reveal any better results and even lead to a high termination rate in the therapy [76]. A sole dietetic attempt through an IgG-adapted elimination before a medicamentous therapy is at any rate justified during consideration of benefit and risks. But at the same time, a consideration of IgE-mediated food allergies and other intolerance is also recommended, since these set similar reaction chains in motion.

An association of fibromyalgia with autoimmune diseases of the thyroid gland is also found. This supports the thesis of an immunologically caused or impressionable fibromyalgia presented here. The therapeutic successes with thyroid hormones in the treatment of these cases is not by any means contradictory, since these hormones influence the metabolism in toto and also assume an immunologically pivotal role [77,78,79].

The clinical picture of fibromyalgia as a complex illness is depicted under consideration of known literature and the results of this paper. Immunological aspects are evident. A step-by-step approach in diagnostics and therapy appears useful. Less invasive procedures which are in the realm of the patient are to be utilized as a priority. Suitable exercise and stress management is also included for this purpose. Analgesics and antidepressants are a consideration in severe or therapy-resistant cases. The clarification of food allergies is part of basic diagnostics. Not only IgE-mediated allergies are to be diagnosed in this connection, but particularly IgG-mediated allergies are also to be disclosed. Particularly on account of the partially very long latency up until appearance of symptoms they are clinically hard to detect and require immunological diagnosis. The statement of IgG diagnosis

is exactly sufficient to be able to give a therapeutic recommendation. Oral provocation tests are generally not necessary. In order to ensure a well-balanced and diversified nutrition, it is necessary to examine a large allergen pool. This has to include all foodstuffs eaten by the patient, otherwise the patient is to continue to incorporate only tested foodstuffs in the diet. Should the success of an IgG-adapted elimination be unsatisfactory, an additional endocrinological diagnosis for thyroid gland – but also for sexual and adrenal hormones – is useful. In addition to the known analgesic and antidepressive medicaments, all complementary techniques are also appropriate, since they have a noticeable benefit for the patients and give them more quality of life.

# 5. Abstract

The results show that nutritionally-specific IgG antibodies are involved in the emergence and/or the severity of a fibromyalgia. Alone the percentage of patients with increased IgG is about 20% higher than during a study conducted on a parallel basis with another collective.

This is emphasized through the high percentage of patients who indicated an amelioration of their complaints through an elimination diet. For instance, the number of very painful pressure points was reduced from 72.1% to 33.8% after an 8-week dietary change. Other symptoms also improved to a similar extent under elimination of foodstuff with increased IgG levels. A large number of test persons even benefited with a not very consistent change. A significant weight loss was shown as a positive side effect. An elimination diet which rests on the avoidance of IgG-positive foodstuffs significantly reduces the complaints of fibromyalgia patients.

A dietary change which avoids foodstuffs with increased IgG levels is successful in the treatment of fibromyalgia. It ameliorated all investigated complaints within 8 weeks by usually more than 50%. In particular, painful events – e.g. migraines, spasmodic abdominal pains, painful defecation, and hyperesthesias of the skin – are subjectively much improved.

In the first two weeks it was especially difficult for the test persons to change their previous eating habits, particularly since “favorite dishes” were frequently affected. In the aggregate, two thirds of the patience assessed their consistency as good to very good. The retention of the new eating habits was much easier for the test persons with continuation of the study. A continual accompaniment of the patients and a good presentation of findings are important for the therapeutic success.

Of the most overweight (41.2%) or obese (29.4%) patients, 86.8% lost an average of 4.7% of their body weight in the observed 8 weeks. An elimination diet which takes into consideration IgG-specific food allergies is successful in weight reduction.

The study participants assessed the success of dietary change as good to very good and were mainly satisfied with the result.

# 6. Conclusion

The greatest challenge in the handling of food allergies and food intolerances is the identification of responsible foodstuffs. Nutrition not only inspires the appetite, but also the emotions. The differentiation of allergic reactions and intolerances is difficult. A clarification with RAST and prick test is not sufficient. A differentiated approach is required. Delayed immunological sequences via IgG play a certain role as trigger of myalgias. An elimination diet which takes into consideration this IgG increase is successful in the treatment of fibromyalgia patients. Observations of other investigators reveal connections between complaints with rheumatic illnesses and fibromyalgia to the ingestion of foodstuffs [25,43,27]. A consistent elimination diet currently represents the only practical management in the treatment of food allergies and complaints triggered as a result. In addition to the classic oral provocation test, the IgG diagnosis is particularly indicated with delayed reactions and as a screening instrument can provide important references for which foodstuff it is worthwhile to make an omission attempt within the framework of an elimination diet. Moreover, it is to be implemented in a low-risk and patient-friendly manner. This is corroborated through the clinical results of the study.

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## 8. Acknowledgments

I would like to express my sincere thanks to Professor Dr. med. Herbert Kellner for the opportunity of dissertation and the very helpful support at all times.

My thanks also go to Mr. Ralf Schierl for the support with the data acquisition and the statistical processing.

I also owe thanks to Mr. Walther Werner for the graphic and linguistic review of the manuscript.

I would like to thank Mr. Gerd Michael Richter for the friendly support and his endless cooperativeness.

I would especially like to thank my wife Anna for the lasting motivation, her understanding and her patience, without which I could not have finished this paper.

# 9. Curriculum vitae

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Born on July 3, 1960 in Rotenburg a.d.Fulda (Germany)

### School and University

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| 1966 | - 1970 | Grundschule Lispenhausen [elementary school] |
| 1970 | - 1979 | Jakob-Grimm-Gymnasium Rotenburg [academic high school] |
| 1979 | - 1980 | Justus Liebig University Giessen |
| 1980 | - 1986 | Georg August University of Göttingen |

Medical internship in *Krankenhaus am Bürgerpark* [Red Cross hospital] , Bremerhaven

### Clinical Activity

| | | |
|---|---|---|
| 1986 | - 1988 | Surgery, Rotenburg Hospital |
| 1988 | - 1989 | Gynecology, Sigmaringen Hospital |
| 1989 | - 1989 | Cardiosurgery, Rotenburg Cardiovascular Center |
| 1990 | - 1990 | General medicine practice, Dr. Grotehans, Bad Hersfeld |
| 1990 | - 2002 | General practitioner with own practice in Rotenburg a.d. Fulda |
| 2002 | - 2003 | Leading physician of the Medical Vital sector of the Medical One AG in Dortmund and Hanover |
| Since November 2003 | | General medicine practice and leadership of the VIP³ MEDICAL CENTER in the Eilenriede Clinic Hanover |

### Main emphases of activity and special expertise

**Acupuncture** German Medical Association for Acupuncture (DÄGfA) diploma and member since 1990

| | |
|---|---|
| **Homeopathy** | Member in the Central Association of Physicians for Naturopathy (ZÄN) since 1990; additional qualification and diploma of the State of Hesse Medical Association: Homeopathy |
| **Environmental Medicine** | Activity in own practice since 1990; additional qualification and diploma of the State of Hesse Medical Association: Environmental Medicine<br>Member in the European Allergy Association (AVE) |
| **Anti-Aging Medicine** | Activity in own practice since 1996; member of GSAAM since 2002; Diplomate of the American Board of Anti-Aging Medicine |
| **Applied Kinesiology** | Activity in own practice since 1998; member and diploma of the German Medical Association for Applied Kinesiology (DÄGAK); member in the International College of Applied Kinesiology (ICAK) |
| **Nutritional Medicine** | Consultation with obesity and metabolic disorders since 1992; certificate: Basic Qualification in Nutritional Medicine from the German Society for Nutritional Medicine |
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| | |
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Hanover, May 24, 2005