BIOLOGICAL THERAPY

JOURNAL OF NATURAL MEDICINE

BT

Reprinted from
Volume X No. 2
pp 237-243.

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by Stefan Zenner, Pharmacist

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by Stefan Zenner, General Practitioner, and Horst Metelmann, Pharmacist

Results of a Multicentric Application Study with 2,409 Patients

Reprinted from the German "Arzneizeitschrift für Naturheilverfahren 3/91, 32nd year

Abstract:

A multicentric application study in the sense of post-marketing surveillance was conducted on 2,409 patients suffering from autonomic dysregulation. The purpose of the study was to determine the effectiveness of therapy with the combination homeopathic preparation Ypsiloheel (in tablet form). The syndrome symptoms which were treated within the context of this study encompassed both somatic and psychic areas. A complex of multiple, different, and simultaneously experienced symptoms was observed among 85.2% of the patients. Therapy took place by administration of Ypsiloheel in individually dosed form, with medicamentous and non-medicamentous adjuvant therapy where necessary. Among the total assessed patient population, therapeutic success (i.e., very good, good, or satisfactory results) was achieved in 91.5% of the cases. In cases treated by Ypsiloheel alone, the rate of therapeutic success was 93.0%. Toleration of Ypsiloheel was very good.

1. Introduction

Autonomic dysregulation occurs relatively frequently among the population of Central Europe. According to Schettler (4), as many as 20-30% of all patients examined in private practices and hospitals suffer in some degree from the complex of disorders designated by autonomic dysregulation. In a study conducted on 780 working men, Bräutigam (1) observed that almost half of them suffered from functional disorders from this syndrome, although they had all been previously classified as healthy.

Autonomic dysregulation can be considered a functional disorder observed in the mechanisms of the autonomic nervous system (2). The interplay between sympathetic and parasympathetic nervous systems — i.e., the equilibrium of these two components of the autonomic nervous system — can with this disease be considered to be disordered. The patient can consequently suffer from a whole complex of various symptoms, including insomnia, headaches, and cardiac difficulties (1 and 4).

The conventional treatment of autonomic dysregulation generally includes physical therapy, as well as psychotherapeutic measures such as autogenous training, patient-centered psychotherapy, and hypnosis. Physicians select the medication typically prescribed for such cases from various and different substance classes; these especially include tranquilizers, other neuroleptic agents, and antidepressants (3).

In addition to orthodox therapy, however, there is a number of preparations with homeopathic constituents which have likewise proved effective in the therapy of autonomic dysregulation. The purpose of this multicentric application study was to assess the effects of the homeopathic combination preparation Ypsiloheel with respect to its therapeutic effectiveness in the treatment of autonomic dysregulation.

2. Methodology employed in testing

2.1 Conduct of the study

A total of 290 registered physicians operating their own practices, with a variety of different specialization fields, took part in the post-marketing surveillance of Ypsiloheel. Before the beginning of data acquisition, the organizers of the study furnished the physicians standard questionnaires for documentation of data on the patients and on the therapy administered. In order to enable as comprehensive evaluation as possible on the patient population treated with Ypsiloheel, no particular inclusion or exclusion criteria were established for the cases to be documented. The individual physicians were entirely responsible for selecting the dosage of Ypsiloheel, the duration of its administration, and the conduct of any adjuvant measures.

Documentation of each case covered by the study included data on the following: age and sex of the patients, as well as precise characterization of each patient's symptom picture. To simplify filling out the data sheet, the questionnaire included 14 different symptoms most frequently encountered within the context of autonomic dysregulation. These symptoms were as follows: cardiac complaints, regulatory disorders of the circulatory system, respiratory difficulties, vertigo or dizziness, headaches, hot flashes, profuse outbreaks of perspiration, globus hystericus, gastrointestinal difficulties, insomnia, anxiety, depressive moods, fatigue, and sexual difficulties. The forms allowed room for the entry of the additional symptoms not on the list. Finally, the physician indicated on the form how long the patient had suffered from the symptom complex before the beginning of the therapy under study.

The physician taking part in the study also recorded the following data on the details of Ypsiloheel therapy: the dosage of Ypsiloheel, the duration of therapy with this preparation, other medicamentous therapy conducted before the beginning of Ypsiloheel treatment, and medicamentous and non-medicamentous adjuvant therapy. In the event that patients had received other medicamentous treatment for autonomic dysregulation before the Ypsiloheel study began, record was made of whether the original medication was continued, reduced, or discontinued after Ypsiloheel therapy began. Each

physician was asked to assess the results of Ypsiloheel therapy by awarding it one of the following grades:

Very good = complete and permanent relief from symptoms

Good = definite and long-term improvement, or complete freedom from complaints for a certain limited time

Satisfactory = temporary improvement

Worsening.

The physicians were requested to indicate any undesired side effects resulting from therapy with Ypsiloheel.

2.2 Processing of the data and statistical analysis

The data were acquired and evaluated with the aid of a suitable computer program. Of the total of 2,430 questionnaires filled out and returned, 21 failed to indicate the type of symptoms or did not give a grade for the results of Ypsiloheel therapy. As a result, they were discarded and not considered in statistical analysis. For all 2,430 patients, however, registration was made of whether or not undesired side effects occurred.

Insofar as possible, the symptoms independently added by the physicians — in addition to those printed on the form — were grouped under one of the already listed, typical symptoms on the questionnaire. For the remaining cases, in which such grouping was not possible, these additional complaints were assigned to the two following, especially-created categories: Not more specifically defined disturbances in general subjective sensations of health, as well as general psychic complaints and miscellaneous complaints.

Representation of the results obtained by statistical evaluation took place partially through basic statistical means, through mean values and standard deviation, as well as partially through indications of absolute or percent frequency distributions. Since not all questions were answered on all questionnaires, the percent values listed do not always add to 100%.

3. Results of therapy with Ypsiloheel

3.1 Description of the patients

Of the 2,409 patients accepted for statistical evaluation, women were represented to a greater degree than men: 68.8% female and 31.0% male cases, with 0.2% without registration of sex. For the entire population, the mean age was 44.04 years (s = ± 17.90) years). For both sexes, the age distribution exhibits a peak in the fifth decade of life. The mean age of women treated with Ypsiloheel was 45.22, which was slightly greater than that of the men: 41.45. Figure 1 graphically depicts age and sex distributions for all patients with complete data given on age and sex (2,104 cases).

Analysis of the symptom pictures for the patients reveals an exceedingly diverse symptom complex, with many and various complaints, for the majority of the population. For more than one-fourth of all cases studied (27.1%), the patients suffered from five or more symptoms simultaneously. A total of 18.1% of the patients complained of four different and simultaneous symptoms; 23.0% of three; and 17.0%, of two. The group of patients for whom only one symptom was registered made up only around one-seventh (14.8%) of the total population (see Figure 2).

Under consideration of both single- and multiple-symptom cases, the most frequent complaints revealed by the study

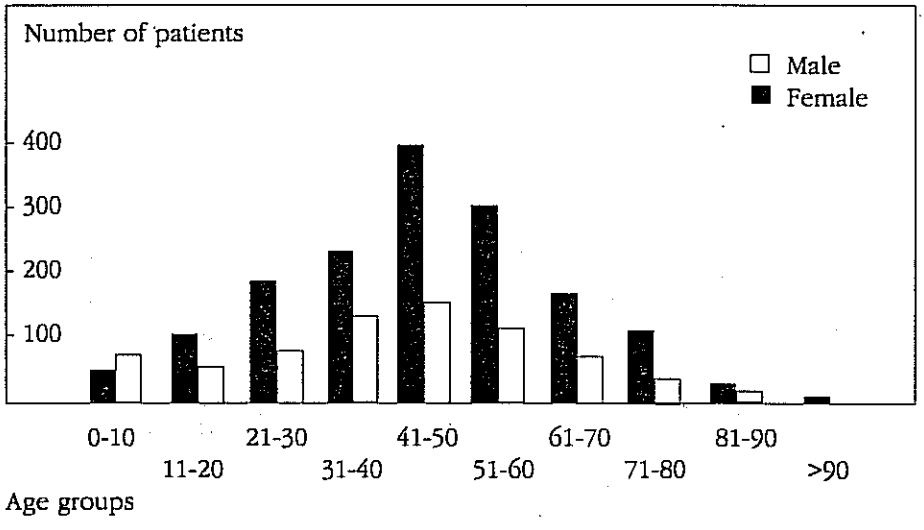

Fig. 1: Patient distribution according to age and sex (n = 2,104)

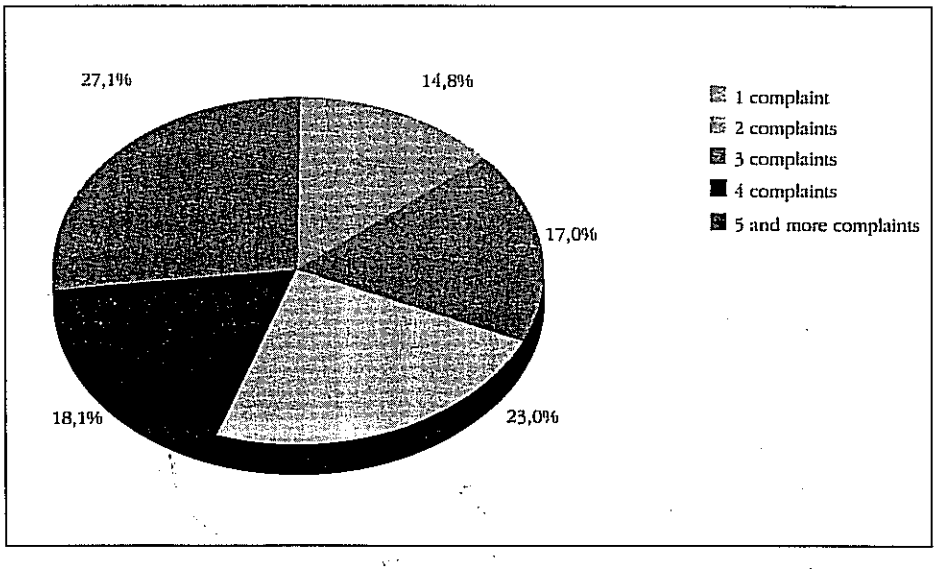

Fig. 2: Number of complaints among patients treated with Ypsiloheel (n = 2,409)

for autonomic dysregulation patients are as follows: insomnia (37.5% of the patients), cardiac complaints (34.2%), vertigo or dizziness (32.0%) and regulatory disorders of the circulatory system (31.7%).

Among all the typical symptoms listed on the questionnaire, sexual difficulties were registered least (8.2%) for the autonomic dysregulation patients in our study. Table 1 lists the data collected for the various complaints, with their sequence according to frequency. The table also shows the absolute frequency and percent of patients with each symptom.

Fifty of the patients (2.1%) complained of symptoms which were assigned to the special additional category designated "Not more specifically defined disturbances in general subjective sensations of health, as well as general psychic complaints." The most specific individual complaints included here were nervousness and emotional unrest. Among the complaints collected in the "miscellaneous" category (58 cases), enuresis nocturna and nausea were relatively frequent.

One conspicuous phenomenon is the following: of all patients for whom only one symptom was registered, the most frequent complaint by far was globus hystericus. From the 356 patients who claimed only one symptom, 29.5% of them suffered from globus hystericus.

There was extremely great variation in the length of time during which patients had suffered from their symptoms until the beginning of Ypsiloheel therapy. With reference to the entire patient population, this term was less than a week in 5.7% of the cases, and between one week and one month for 32.0% of the patients. Complaints lasting longer than one month but less than a year were suffered by 36.5%. Symptoms of longer than a year were registered for 25.6% of the cases treated and covered by this study.

Table I: Listing of complaints according to the frequency of their appearance in the study (single- and multiple-symptom cases)

Symptom	Absolute no. of patients suffering from each of the complaints	Percent of total no. of patients with each symptom
Insomnia	904	37.5 %
Cardiac complaints	825	34.2 %
Vertigo or dizziness	772	32.0 %
Regulatory disorders of the circulatory system	763	31.7 %
Depressive moods	743	30.8 %
Anxieties	721	29.9 %
Headaches	717	29.8 %
Globus hystericus	691	28.7 %
Profuse outbreaks of perspiration	527	21.9 %
Gastrointestinal complaints	517	21.5 %
Fatigue	495	20.5 %
Heat flashes	368	15.3 %
Respiratory difficulties	367	15.2 %
Sexual difficulties	197	8.2 %
Miscellaneous complaints	58	2.4 %
Not more specifically defined disturbances and general subjective sensations of health, as well as general psychic complaints	50	2.1 %

3.2 Medication

The preparation Ypsiloheel was furnished to us by its manufacturer in tablet form, with standard recommendation for sublingual administration. The physicians participating in our study were, however, naturally allowed complete freedom in prescribing dosage. At the end of the study it became apparent, nevertheless, that the great majority of surveyed patients (76.6%) took Ypsiloheel approximately in accordance with the manufacturer's recommendations: one tablet, sublingually, three times a day. Dosage was more than three tablets a day for 19.4% of the patients, and less than three tablets for 3.6%.

Before the beginning of surveyed Ypsiloheel administration, 1079 of the patients (44.7%) had already taken other medication for treatment of the same symptom complex. In 678 cases, the physicians participating in our survey obtained precise information on the manner of previously administered medicamentous therapy. The surveyed patients had for the most part taken preparations from one or more of three basic groups: tranquilizers, neuroleptic agents, and antidepressants. In analysis of only those patients who had earlier taken medication from any one single substance group of these three basic possibilities, the following was determined: tranquilizers had been prescribed in by far the most of these cases (for 306 patients), with antidepressants

second (183 cases), and neuroleptics third (52). Medication from various other substance groups had been prescribed for 30 additional patients. Combinations of several preparations from more than one substance class had been used by 107 patients.

Upon analysis of data from this study, it was especially interesting to determine the answer to the following questions: was it possible, during the course of treatment with Ypsiloheel, to reduce or to terminate administration of this previous medication? Or was the original medication continued as before? After careful analysis of data gained from the surveyed patients, it became clear that, as a result of therapy with Ypsiloheel, a reduction in use of their medicinal products was indeed possible in a considerable share of the cases. Among 306 patients who had been earlier treated with tranquilizers, for example, 40.8% were able to do without further administration of their original medication. For a further 48.0% dosage reduction in earlier-taken preparations was possible. Table II indicates the percent of patients for whom previous medication was able to be reduced or discontinued. These data include changes in use of the three most prevalent substance groups: tranquilizers, neuroleptic agents, and antidepressants (only patients who in each case had taken only one of these three). From these data, it may be concluded that, at least for a considerable share of patients suffering from autonomic dysregulation, the homeopathic combination preparation Ypsiloheel can in fact represent a genuine alternative to chemically defined pharmaceuticals.

The duration of therapy with Ypsiloheel was between one week and three months for the majority of surveyed patients. Therapy was terminated before the end of one week for only 3.9% of the entire population. Almost half of the patients included in the post-marketing survey (49.7%) received treatment in the form of Ypsiloheel for more than one week, but no longer than one month. An additional third (34.6%) received Ypsiloheel for a period of between one and three months. Therapy lasting from three to six months was conducted with 9.1% of the patients, and 1.8% took the preparation more than six months.

Table II: Changes in previous medication after beginning of therapy with Ypsiloheel

Type of previous medication	Tranquilizers	Antidepressants	Neuroleptics
Number of patients	306	183	52
Retention of previous medication at the former level (in %)	11.1 %	20.8 %	17.3 %
Dosage reduction of the previous medication (in %)	48.0 %	51.4 %	34.6 %
Discontinuation of the previous medication (in %)	40.8 %	27.3 %	44.2 %

After correlation of the period of therapy to the length of time during which the respective patients had suffered from symptoms of autonomic dysregulation, it was revealed that, in general, the longer the symptom complex had prevailed among the individual patients before the survey, the longer the therapy with Ypsiloheel lasted. Patients with a relatively short history of complaints (up to one month) took Ypsiloheel no longer than one month in 78.5% of the cases. The figures were different for patients who had suffered from their complaints longer than one month and less than one year. Among this subgroup, Ypsiloheel therapy of one month or less was sufficient in only 44.7% of the cases, with longer therapy necessary for the remainder of patients (54.4%). If the syndrome had prevailed for longer than one year, 69.0% of the patients involved took the preparation for more than one month.

3.3 Administration of adjuvant therapy

For 1,460 of 2,409 patients (60.6%), adjuvant therapy was administered for treatment of the same symptom picture which had prompted administration of Ypsiloheel. In 627 of these cases, additional therapeutic measures were restricted to non-medicamentous procedures: generally, psychotherapy and/or physical therapy. Simultaneous medicamentous and non-medicamentous adjuvant therapy was provided for 499 patients. Strictly medicamentous therapy, in addition to Ypsiloheel, was received by 334 patients.

Homeopathic preparations represented the largest classification of medication administered as adjuvants: 32.4% of 833 patients received homeopathic agents in addition to Ypsiloheel. The second most frequently prescribed adjuvants were phytomedicines (22.3%), followed by tranquilizers (20.9%), cardioactive agents (2.6%), and gastrointestinal preparations (2.4%).

Non-medicamentous adjuvant measures consisted basically of client-centered therapy (62.9% of 1,126 cases with non-medicamentous adjuvant therapy), physical therapy (28.1%), and autogenous training (18.5%). Owing to numerous cases in which more than one type of therapy was registered, the sum of the individual percent figures here is more than 100% in each case.

3.4 Results of therapy

Results of *very good or good* were achieved in 69.5% of the total, evaluated patient population. An additonal 22.0% of the patients obtained satisfactory results. One may therefore conclude that therapeutic success was possible for a total of 91.5% of all patients. The remaining 8.5% of attempts must be assessed as failures, since no improvement was registered — or, as occurred in 5 cases (0.2% of the patient population), since worsening of the patient's existing condition was observed at the same time that Ypsiloheel therapy took place (see Figure 3).

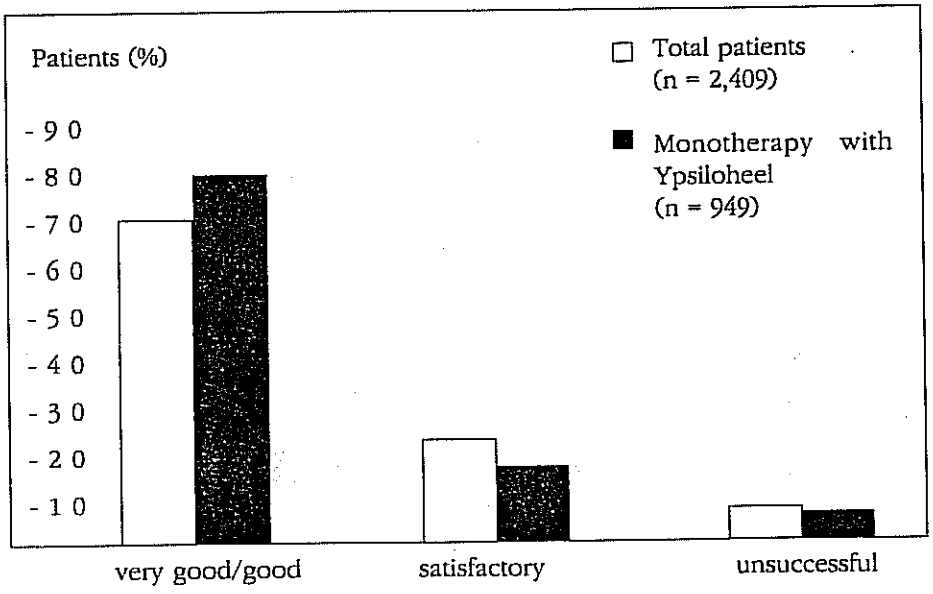

Fig. 3: Therapeutic results among patients treated with Ypsiloheel (n = 2,409)

Among the patients who received only Ypsiloheel therapy, i.e., without medicamentous or non-medicamentous adjuvants, the share of *very good and good* therapy results was 76.1%: somewhat higher than the rate in the total population. If the additional subgroup of 16.9% with *satisfactory* therapy results is also included as successful, then the rate of successful therapy strictly with Ypsiloheel is 93.0%. This extremely high rate may be suspect upon first consideration, but can with all probability be satisfactorily explained, at least in part, by the following fact: that the cases treated exclusively with Ypsiloheel represented, as a rule, symptom complexes which were relatively less severe and therefore more amenable to therapy. At the same time, however, these results also impressively verify the effectiveness of Ypsiloheel. Indeed: the documented therapy success achieved here by Ypsiloheel alone — with 949 cases, representing almost 40% of the entire patient population — was all the more striking in that it could not have been contributed to or influenced in any other way by adjuvant therapeutic efforts.

Upon comparative analysis among the various subgroups of the total patient population, with assessment of the relationship between length of symptom prevalence and success of therapy, the following general correlation was found: the shorter the previous history of suffering from autonomic dysregulation symptoms, the better the results of therapy. Patients who had experienced less than one week of complaints achieved a relatively high rate of therapeutic success: results for 88.3% of this subgroup were graded *very good or good*. Once the syndrome had prevailed between one week and one month, the rate for *very good or good* was 77.3% of all cases. For symptoms lasting between one month and one year, this same success rate was 70.8%, and for patients who had suffered longer than one year, 53.6%.

Among those patients who had received no other medicamentous therapy for treatment of autonomic dysregulation before receiving Ypsiloheel for the same purpose, the physician in charge of therapy assessed 75.6% with *very good or good* ratings. Of all patients, on the other hand, who had received other medication before starting Ypsiloheel, the *very good or good* rate was only 62.0%. The following finding was, however, highly noteworthy: in those cases in which the previously administered medication was completely discontinued during therapy with Ypsiloheel, the physicians registered *very good or good* results for 79.1% of the patients.

Further analysis of the findings of this study was conducted to determine the relative extent to which individual symptom constellations were particularly amenable to treatment by Ypsiloheel. Accordingly, Table III was prepared to show the ranking of individual symptoms, each of which had received evaluations of *very good or good* for therapy results. The percent frequency of *very good or good* grading ranged between 50.0% and 72.8% for the individual complaints. At the upper, most successful, end of the scale were the following symptoms: globus hystericus, regulatory disorders of the circulatory system, cardiac complaints, and headaches. At the lower, least amenable end, were the following: fatigue, depressive moods, not more specifically defined disturbances in general subjective sensations of health and general psychic complaints, as well as miscellaneous symptoms.

Whereas Table III depicts the therapy results with respect to all responses for symptoms (both single and multiple indications of symptoms), Table IV illustrates the outcome of therapy for each symptom, but with consideration only for the subgroup of patients who had indicated merely one symptom within the syndrome of autonomic dysregulation. As in Table III, the symptom data shown here is ranked from the top down according to the degree of therapeutic success. To save space, however, only those symptoms are listed in Table IV for which at least 10

Table III: Ranking of individual symptoms, according to their achievement of "very good" and "good" results (single and multiple responses)

Symptom	Absolute no. of patients suffering from each of the complaints	Percent of total no. of patients who achieved "very good" or "good" results for each symptom
Globus hystericus	691	72.8 %
Regulatory disorders of the circulatory system	763	71.8 %
Cardiac complaints	825	71.3 %
Headaches	717	70.5 %
Profuse outbreaks of perspiration	527	69.8 %
Insomnia	904	68.8 %
Anxieties	721	68.7 %
Vertigo or dizziness	772	68.6 %
Gastrointestinal complaints	517	68.5 %
Respiratory difficulties	367	67.8 %
Sexual difficulties	197	67.5 %
Heat flashes	368	67.2 %
Fatigue	495	65.9 %
Depressive moods	743	63.8 %
Not more specifically defined disturbances in general subjective sensations of health, as well as general psychic complaints	50	56.0 %
Miscellaneous complaints	58	50.0 %

treated cases had been documented. At the top, most successful end we find regulatory disorders of the circulatory system and headaches, and at the lower, least successful end we have anxieties and depressive moods.

Further analysis of therapy results with Ypsiloheel as broken down by the number of registered complaints reveals that the percent of cases with 1 - 5 simultaneously experienced symptoms which achieved *very good or good* therapy results lies within the following range: 68.4 - 71.6%. For cases with 6 - 8 symptoms, the rate for the same successful results was 62.3 - 64.4%. For patients with more than 8 symptoms, greater success rates were in many cases registered: up to 83.3% *very good or good* results. These data indicate that Ypsiloheel is in fact an effective therapeutic agent even for syndromes with numerous different symptoms.

3.5 Patient tolerance of Ypsiloheel

Within the context of this post-marketing survey, it was observed and documented that nine of the patients possibly suffered undesired side effects during the same period in which they took Ypsiloheel. In one case with moist ear eczema on the right lobe, the physician immediately recognized that there was no apparent causal relationship between the eczema and administration of Ypsiloheel. Three patients reported experiencing fatigue after taking Ypsiloheel. This phenomenon is not necessarily due to any sedative effects of the medication, however: it may well be the expression of an already existing sleep deficit of the patients which the organism attempted to compensate for as a result of therapy with Ypsiloheel. In addition, there was one report of undesired effects for each of the following symptoms: headache, slight nausea with temporary headache, slight itching, moderate nausea, and allergy with rash on the upper arm. These very few symptoms, among the great number of patients in the survey, merely involve slight and subjectively assessed complaints. In addition, no proof of a causal connection has been established between these registered symptoms and administration of Ypsiloheel. It is also well possible that the complaints which turned up here may actually represent symptoms of the basic illness being treated, autonomic dysregulation, and that they cannot be traced to the medicamentous therapy.

4. Evaluation of data from the study on Ypsiloheel

Post-marketing surveys enable documentation, under conditions of daily medical practice, of the therapeutic employment of licensed and registered medication already on the market. In addition, such studies provide insights into customary and accepted usage of a particular remedy: for example, for which symptom pictures or individual complaints it can be successfuly used, and with which adjuvant measures it may satisfactorily be combined. Such studies also, of course, provide reliable verification of the actual results achieved by a particular medication.

The complaints treated with Ypsiloheel in the context of this survey were many and varied in nature and covered a wide range of symptom areas: including those

Table IV: Ranking of individual symptoms, according to their achievement of "very good" and "good" results (only single-symptom responses)

Symptom	Absolute no. of patients suffering from each of the complaints as mono-symptom	Percent of mono-symptom patients who achieved "very good" or "good" results for each symptom
Regulatory disorders of the circulatory system	25	96.0 %
Headaches	22	81.8 %
Gastrointestinal complaints	52	78.8 %
Insomnia	31	77.4 %
Vertigo or dizziness	14	71.4 %
Cardiac complaints	24	70.8 %
Globus hystericus	105	69.5 %
Anxieties	19	63.2 %
Depressive moods	21	42.8 %

clearly with somatic components (cardiac complaints and regulatory disorders of the circulatory system) and those obviously of psychic nature (anxieties and depressive moods). The following information provided in this survey serves as an indicator for the severity of the symptom complex encountered: number and duration of symptoms, previous and adjuvant medicamentous therapy, additional physical and psychotherapeutic measures, and the duration of therapy.

The physicians participating in this survey attested comparatively better effectiveness to Ypsiloheel for the treatment of complaints with a short history, with definite somatic components, and with the apparent capability of being treated by Ypsiloheel alone (i.e., for which adjuvant therapy was not considered). Ypsiloheel results were especially favorable for these cases, as compared to those characterized by long-lasting complaints as well as by pronounced psychic components, against which other therapeutic measures had already been tried and for which Ypsiloheel was employed in addition to other methods of treatment. A long history of symptoms, previous medication, and adjuvant therapy are, in any case, indications for heightened severity in such symptom complexes. As a result, it is completely logical that therapeutic success rates will be lower for such syndromes than for less severe illnesses of shorter duration.

According to the results obtained from this study, patient tolerance of Ypsiloheel may be assessed as very good. Of the total of 2,430 patients covered, only nine reported undesired effects. In all cases, these possible side-effect symptoms were of minor degree, and their causal relationship to Ypsiloheel therapy must be considered more or less questionable in all cases. The following factors are of significance when making risk-benefit considerations for Ypsiloheel: the extremely low side-effect rate, the fact that administration of Ypsiloheel makes it possible to reduce the dosage of more pharmaceutically powerful substances, and the possibility in many cases of treating patients with autonomic dysregulation by means of Ypsiloheel alone.

In general summary, it may be concluded that the post-marketing survey described here verifies that Ypsiloheel is applicable over a broad application area, with reliable effectiveness, and with very good patient tolerance.

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Address of the authors:

Stefan Zenner, M.D.
Ahornstrasse 7
W-7573 Sinzheim
Germany

Horst Metelmann, R.Ph.
Gellertstrasse 24
W-7500 Karlsruhe 21
Germany