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A Randomized Double-blind Controlled Clinical Study

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A Randomized Double-blind Controlled Clinical Study

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Objective: To compare the efficacy and safety of a homeopathic remedy (Vertigoheel, Heel Inc, Albuquerque, NM) vs betahistine hydrochloride (active control) in the treatment of patients with vertigo of various origins in a confirmative equivalence trial.

Design: Randomized (1:1) double-blind controlled clinical trial.

Setting: Fifteen study centers (general practice) in Germany between November 1995 and November 1996.

Subjects: A total of 119 patients with vertigo of various origins (from whom 105 patients could be analyzed as intended per protocol).

Main Outcome Measures: Frequency, duration, and

intensity of vertigo attacks.

Results: Both homeopathic and conventional treatments showed a clinically relevant reduction in the mean frequency, duration, and intensity of the vertigo attacks. The therapeutic equivalence of the homeopathic remedy and betahistine was established statistically.

Conclusions: Concerning the main efficacy variable, therapeutic equivalence between the homeopathic remedy and betahistine could be shown with statistical significance (confirmative analysis). Both remedies reduced the frequency, duration, and intensity of vertigo attacks during a 6-week treatment period. Also, vertigo-specific complaints were significantly reduced in both treatment groups.

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VERTIGO IS a common symptom with significant adverse effects on the patient's quality of life. Physicians in private practice are frequently confronted with this diagnosis, which often requires extensive investigation to determine its origin. In one study,¹ dizziness was the ninth most common symptom at initial evaluation in the outpatient setting. Vertigo may arise from lesions in the central nervous system, particularly in the nuclei of the vestibular nerve, the cerebellum, and the connections between cerebellar and vestibular nuclei. More frequently, vertigo is caused by disturbances of the vestibular nerve and vestibular cochlear system and occasionally is of vascular origin.² Vertigo results from abnormal processing of apparently contradicting information in the central nervous system and is often accompanied by auditory symptoms, making it more difficult for the patient to tolerate. Patients with vertigo suffer from nausea, emesis, sweating, collapse, and tinnitus. Disturbances of equilibrium, includ-

ing rotational or positional vertigo, systematic imbalance, or instability, can have negative consequences on the social lives of patients and can be truly disabling.

Benign paroxysmal positional vertigo, vestibular neuritis, and Ménière disease are the primary types of vertigo, but the exact cause of vertigo often remains unknown. In many patients, a further complicating factor is that the vertigo symptoms continually change character and intensity. Positional vertigo is usually indicative of a benign vestibular disorder. The most common type is benign paroxysmal positional vertigo, which is characterized by a feeling of dizziness while lying down as well as in the sitting position. There may be dizziness from turning the head from side to side or from flexing and extending the neck. The classic finding on examination is a burst of rotary nystagmus when the patient is rapidly placed in the right- or left-ear-down position.² Regardless of the exact cause, it is important to reduce the frequency, intensity, and duration of vertigo attacks with an effective medication that has no adverse effects.

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PATIENTS AND METHODS

Between November 1995 and November 1996, 119 patients of both sexes from 15 centers (all general practices) in Germany were considered for enrollment in the study. The main inclusion criteria were acute or chronic vertigo symptoms of various origins (including Ménière disease and vasomotor vertigo), a minimum of 3 vertigo attacks during the week before the study began, and an assessment of intensity of vertigo attacks by the patient between 2 and 4 on a 5-point rating scale (see below). The main exclusion criteria were chronic vertigo (longer than 6 months) if specifically treated during the 4 weeks before the study began; vertigo caused by psychovegetative disorders (to avoid possible noncompliance); vertigo caused by a tumor or coffee, tea, tobacco, alcohol, or drug abuse; vertigo caused by inflammation from an underlying disease; myocardial infarction within 6 months before the study began; severe metabolic disease; gastroduodenal ulcer; pheochromocytoma; or bronchial asthma. Furthermore, other concomitant vertigo or antiemetic medication, corticosteroids or antihistamines, migraine medication, psychoactive drugs, and vascular drugs were not allowed during the study (wash-out phase, 7 days before the study began). The study was conducted in accordance with Good Clinical Practices, consistent with the Declaration of Helsinki, and the product was manufactured in accordance with Good Manufacturing Practices, consistent with the US Food and Drug Administration's Code of Federal Regulations. The study was conducted by a contract research organization to exclude the possibility of a sponsor bias.

After being screened for eligibility, patients were randomly assigned to the homeopathic-remedy group or the betahistine group (day 1 = visit 1). Randomization was performed at each center by assigning consecutive patients to the next available treatment group from a computer-generated randomization list. The study was double blind, consistent with the "double-dummy" technique¹³: because of the difference in taste between betahistine and the homeopathic remedy, corresponding placebos of the active drugs were produced that were identical in taste, as well as shape and smell. The patients in both groups took 15 drops 3 times

daily of the active drug (homeopathic remedy or betahistine) plus the corresponding placebo each day for 42 consecutive days (betahistine dosage: 18 mg/d in 3 divided doses). Effectiveness and tolerability of the treatments were checked at day 3 (± 1 day, visit 2), day 7 (± 1 day, visit 3), and after days 14 (± 2 days, visit 4), 28 (± 3 days, visit 5), and 42 (± 3 days, visit 6). To assess the influence of the treatment on quality of life, the patients were advised to continue normal physical activity (see below). Laboratory tests and physical examinations were conducted for each patient at the beginning (day 1) and end (day 42) of the study.

PRIMARY EFFICACY VARIABLES

Frequency, duration, and intensity of vertigo attacks were the primary efficacy variables. These variables were assessed at visit 1 for the week before the study began (baseline) and for each study day in a diary. The mean daily duration of all vertigo attacks was assessed on a 5-point rating scale, where 0 indicates between 0 and 2 minutes; 1, between 2 and 10 minutes; 2, between 11 and 60 minutes; 3, between 1 and 6 hours; and 4, more than 6 hours. The mean daily intensity of all vertigo attacks was assessed on another 5-point rating scale, where 0 indicates no discomfort; 1, slight discomfort; 2, moderate discomfort; 3, severe discomfort; and 4, very severe discomfort. For all 3 variables, the mean daily occurrences of all vertigo attacks were assessed by the patient on an ordinal rating scale.

SECONDARY EFFICACY VARIABLES

Quality of Life

The quality of life was measured at visits 1 and 6 (at the last visit for patients who did not complete the study) with the validated questionnaire Medical Outcome Study-Short Form 36.¹⁴ This questionnaire provides a comprehensive, psychometrically sound and efficient way to measure health from the patient's point of view by scoring standardized responses to standardized questions concerning physical health (physical functioning, role limitations attributed to physical problems, bodily pain, and general health) and mental health (vitality, social functioning, role

The following clinical trial involves a homeopathic preparation (Vertigoheel, Heel Inc, Albuquerque, NM) containing ambra grisea D6, anamirta cocculus D4, conium maculatum D3, and petroleum rectificatum D8. (Designators D6, D4, D3, and D8 denote the concentrations of the various ingredients of the homeopathic preparation.) This homeopathic remedy has been applied successfully in the treatment of vertigo in earlier studies.³⁻⁵ The mode of action of the homeopathic remedy is not fully understood. However, its pharmacodynamic effects on acoustically evoked brainstem potentials have been investigated.⁶ The present study was designed to test the therapeutic equivalence of the homeopathic remedy vs betahistine hydrochloride. Betahistine (2-pyridine) stimulates the histaminergic histamine 1 and histamine 2 receptors in the brain, which increases the cyclic adenosine monophosphate (cAMP) levels in the blood vessel walls. As a result, blood flow, especially in the brain, is

increased through vasodilation. Betahistine is considered a standard treatment for patients experiencing vertigo.⁷⁻¹⁰ Its efficacy has been determined in previous placebo-controlled studies.^{11,12} Therefore, betahistine was chosen as the reference drug for this clinical trial.

RESULTS

A total of 119 patients (59 in the homeopathic group and 60 in the betahistine group) were recruited, randomized, treated, and observed in 15 centers. The number of patients per center varied between 1 and 23. The data of 2 patients were inconsistent and not comprehensible and, therefore, were excluded from the study. Major protocol deviations (violations of inclusion or exclusion criteria, compliance, premature study termination because of patient's personal reasons, or unavailable for follow-up) led to the exclusion of 12 patients from analysis intended per

limitations attributed to emotional problems, and mental health). The version translated to German and psychometrically tested was used in this study. For the questionnaires, transformed raw scores were computed according to the Medical Outcome Study-Short Form 36 manual.¹⁴

Severity and Impact

Severity of vertigo-specific symptoms and general impairment of daily life were assessed by means of a questionnaire that was based on the Neuro-Otologische Datenerfassung Claussen test,^{3,4,6} a specific anamnestic rating scale for patients with vertigo. The questionnaire was divided into 4 parts, each containing a different set of questions. Set 1 assessed the direct vertigo symptoms, such as feeling of spinning, staggering, or elevation. Set 2 assessed the intensity of vertigo during different special exercises, such as turning the head, bending down, getting up, and laying down. Set 3 assessed vertigo-associated symptoms, such as general weakness, restrictions in hearing or seeing, headache, tinnitus, tiredness, anxiety, or insomnia. Set 4 assessed restrictions in daily life activities, such as problems while reading, going up or down stairs, using public transportation, performing housework, or walking in the dark. A total score was calculated from the scores of the individual questions and transformed to a scale of 0 (maximum number of symptoms) to 100 (no symptoms) for comparability.

ASSESSMENT OF EFFICACY

The patients' and investigators' global assessments of efficacy were carried out on a 5-point rating scale, where 1 indicates absolutely no complaints; 2, significant improvement; 3, slight improvement; 4, no improvement; and 5, deterioration.

The safety of the study medications was assessed by means of adverse events, clinical laboratory data (hematologic evaluations, clinical chemical evaluations, and urinalysis), and vital signs (blood pressure, pulse, body weight, and oral body temperature). Finally, the investigators and the patients assessed the global overall tolerability of the treatment at visit 6 according to the following scale: 1 indicates excellent; 2, good; 3, fair; and 4, poor.

STATISTICS

The sample size was calculated on the basis of the following assumptions: mean score reduction of 2 points in intensity of vertigo attacks while taking betahistine; assumed SD of score reduction, 0.8; probability of falsely rejecting the hypotheses of inferiority of homeopathic remedy, $\alpha = .05$; and power of the test, $1 - \beta = 0.8$. The region of equivalence was stipulated at 20% (ie, a minor reduction of 0.4 score points). These assumptions mandated 50 patients per treatment group to demonstrate the equivalence of the homeopathic remedy and betahistine. Primary variables for the assessment of efficacy were the reduction of frequency, duration, and intensity of vertigo attacks, defined as the difference between the mean daily occurrences during the last study week (week 6) and the week before the study began (baseline). It was expected that the differences for the 3 variables would develop in the same direction (1-sided *t* test). The Weibull-Lachin directional test¹⁵ was performed as a simultaneous test to control the α level of .05. As a measure for effect size, the Mann-Whitney test was used (probability of superiority or inferiority of a patient in the homeopathic group compared with a patient of the betahistine group). Therefore, only ordinal information was used to assess treatment effects, reducing the possibility of biasing the treatment results because of the nonlinearity of scaling distances. The following hypotheses were stipulated in the trial protocol to show the noninferiority of the homeopathic group to the betahistine group: The treatment difference (homeopathic product minus betahistine) was equal to the lower equivalence margin for the reduction of frequency, duration, and intensity of vertigo attacks vs the alternative that the treatment difference was greater than the lower equivalence margin for at least 1 of the primary efficacy variables. Equivalence or superiority of the homeopathic remedy vs betahistine was shown if the lower limit of the 95% confidence interval (1-sided) of the Mann-Whitney statistic is larger than 0.36 (ie, moderate inferiority). The test was carried out using the validated program SmarTest.¹⁵⁻¹⁷ The last-observation-carried-forward principle was used to include patients who did not complete the study (owing to cure or other reasons) in the analysis (end-point analysis). The secondary efficacy variables and the safety variables were analyzed descriptively.

protocol analysis. The per protocol analysis was chosen as the primary efficacy evaluation, because it is the more conservative analysis in equivalence trials.¹⁸ A total of 117 patients were assessed with regard to safety. Of the 105 patients in the per protocol analysis, 9 patients (8.6%) terminated the study prematurely because of cure (homeopathic group, $n = 4$; betahistine group, $n = 3$) or worsening of symptoms (betahistine group, $n = 2$). The patients in the 2 treatment groups were comparable with regard to demographic (eg, sex and age) and anamnestic (eg, abnormal findings at baseline or characterization of vertigo) data. In only a small percentage (approximately 10%) was the exact cause of vertigo known (eg, cardiovascular disease or orthostatic hypotension). In more than 70% of the patients in both treatment groups, the patients were being treated for vertigo for the first time. Patients with differential diagnoses were enrolled in the study with vestibular vertigo (rotary vertigo, positional vertigo, elevation-

induced vertigo, or staggering vertigo), vasomotor vertigo (caused by circulation disturbances, eg, arteriosclerosis, hypertension, or hypotension), or both (Table 1). Whereas vestibular vertigo has a clear direction of motion (eg, rotary vertigo or elevation-induced vertigo), the vasomotor vertigo is more diffuse (eg, blurred vision or unsteadiness). The mean exposure time to treatment was 40.2 days (homeopathic remedy) vs 40.9 days (betahistine) in the per protocol analysis. In the safety population, the mean exposure times were 39.3 days (homeopathic remedy) and 37.6 days (betahistine).

PRIMARY EFFICACY VARIABLES

The therapeutic equivalence of the homeopathic remedy and betahistine was demonstrated statistically by analyzing the primary variables. The values of the primary variables revealed no significant differences between the

Table 1: Baseline Characteristics for Patients in the Evaluable Efficacy Sample

Parameters	Homeopathic Group (n = 53)	Betahistine Group (n = 52)
Sex, No. (%)		
Male	16.0 (30.2)*	13.0 (25.0)*
Female	37.0 (69.8)	39.0 (75.0)
Age, y		
Mean (SD)	50.0 (16.3)†	54.8 (15.9)†
Median (range)	49.0 (18.0-77.0)	57.0 (26.0-83.0)
Patients with abnormal findings, No. (%)‡	23.0 (39.7)	23.0 (39.0)
Patients receiving prestudy or concomitant medication, No. (%)§		
Yes	17.0 (32.1)	18.0 (34.6)
No	36.0 (67.9)	34.0 (65.4)
Characterization of vertigo, No. (%)		
Vestibular vertigo	29.0 (54.7)	35.0 (67.3)
Vasomotor vertigo	19.0 (35.8)	11.0 (21.2)
Both	5.0 (9.4)	6.0 (11.5)
Cause of vertigo, No. (%)		
Known	7.0 (13.2)	5.0 (9.6)
Unknown	46.0 (86.8)	47.0 (90.4)
First-time treatment of vertigo, No. (%)	39.0 (73.6)	39.0 (75.0)
Chronic or relapsed vertigo, No. (%)	14.0 (26.4)	13.0 (25.0)
Time since first occurrence of vertigo symptoms, mo, median (range)	1.3 (0.1-309.0)	1.8 (0.1-154.0)

*P = .66 by Fisher exact test.

†P = .17 by Mann-Whitney test.

‡These patients had abnormal findings (eg, problems in the musculoskeletal system or head and nape or with vascular state) at the baseline physical examination.

§Medication for treatment of abnormal findings above.

||Vasomotor vertigo caused by circulation disturbances (eg, arteriosclerosis, hypertension, or hypotension).

homeopathic group and the betahistine group before the start of treatment (baseline) and during the last study week. In all 3 primary variables, a clinically relevant reduction was found (**Figure 1** and **Table 2**). The alternative hypothesis of noninferiority of the homeopathic remedy concerning at least 1 of the 3 vertigo criteria can therefore be accepted (Mann-Whitney statistics: $P[X < Y] = .51$ with a lower 1-sided 95% confidence limit = 0.46). Concerning the frequency of vertigo attacks, a slight superiority of the homeopathic remedy in comparison to betahistine could be ascertained (Figure 1). Concerning the criteria of duration and intensity of vertigo attacks, no marked difference between the treatment groups could be ascertained. For both variables, the lower 1-sided 95% confidence limit was greater than the limit of a mean inferiority (**Figure 2**).

SECONDARY EFFICACY VARIABLES

In all 4 categories of the vertigo-specific questionnaire, there was a significant reduction of the vertigo-specific symptoms. No marked differences were found between the 2 treatment groups (**Table 3**). The descriptive results for the quality-of-life questionnaire Medical Out-

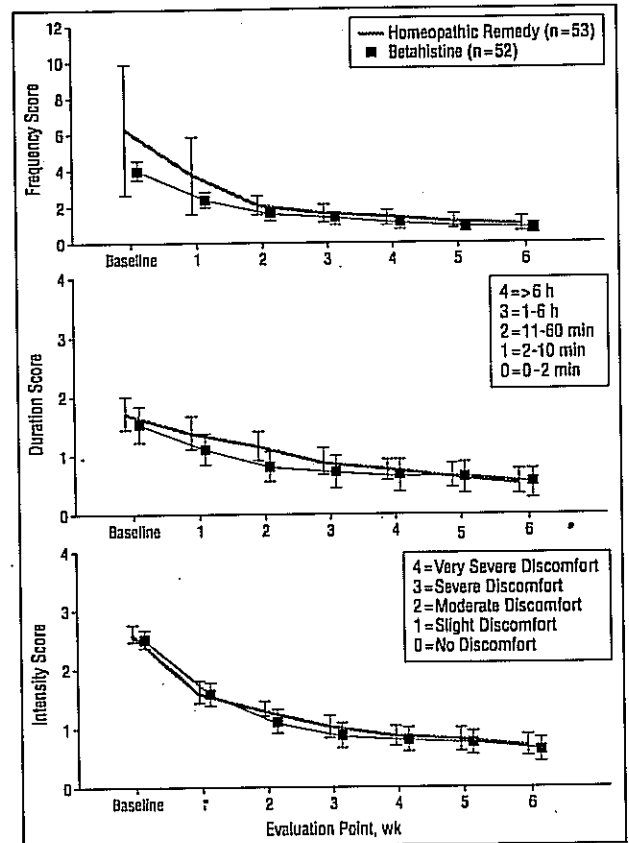


Figure 1. Mean daily frequency, duration, and intensity of vertigo attacks at baseline through week 6 are shown. Error bars indicate upper and lower 95% confidence limits.

come Study-Short Form 36 are summarized in **Table 4**. Overall, in all categories of physical and mental health, an increase from baseline to visit 6 (or the last visit for patients not completing the study) can be seen. There are no striking differences between the treatment groups. The global assessment of efficacy by the investigators and the patients did not reveal striking differences between the 2 treatment groups (Mann-Whitney test, 1-sided: investigators, $P = .63$; patients, $P = .76$). A worsening of symptoms was seen in 1 (1.9%) patient (investigators' assessments) and 3 (5.8%) patients (patients' assessments) with betahistine treatment, whereas no worsening of symptoms was seen with the homeopathic treatment. In both groups, for more than 70% of the patients a significant improvement with absolutely no complaints was reported by the investigators.

SAFETY VARIABLES

Fifty-seven adverse events (29 in the homeopathic group and 28 in the betahistine group) during the clinical trial were reported for 31 patients (26.5%). The causal relationship of an adverse event to the study treatment was assessed by the investigator as very probable, probable, or possible 4 times in 2 patients (homeopathic group, 3.4%) and 2 times in 1 patient (betahistine group, 1.7%). The specific adverse events were nausea, tremor of the hands in the homeopathic group, and headache combined with very strong vertigo in the betahistine group.

Table 2. Mean Frequency, Duration, and Intensity of Vertigo Attacks per Day in the Evaluable Efficacy Sample*

Statistics	Frequency of Vertigo Attacks†		Duration of Vertigo Attacks†		Intensity of Vertigo Attacks†	
	Baseline	Change	Baseline	Change	Baseline	Change
Homeopathic group score (n = 53)						
Mean (SD)	6.3 (13.1)	-5.3 (13.3)	1.7 (1.0)	-1.2 (1.2)	2.6 (0.5)	-1.9 (0.8)
Median	4.0	-3.4	2.0	-1.0	3.0	-1.9
Betahistine group score (n = 52)						
Mean (SD)	4.0 (1.8)	-3.3 (2.1)	1.5 (1.1)	-1.0 (1.4)	2.5 (0.5)	-1.9 (0.8)
Median	4.0	-3.0	1.0	-1.0	2.0	-2.0
P, Mann-Whitney test	.163230	...
P (X < Y)‡	0.42	...	0.45	...	0.45	...
95% CI‡	0.31 to 0.53	...	0.34 to 0.55	...	0.35 to 0.55	...
Single test‡						
P (X < Y)	...	0.53	...	0.51	...	0.50
90% CI, LBS§	...	0.46	...	0.44	...	0.43
Simultaneous test						
P (X < Y)‡	0.51
90% CI, LBS§	0.46

* See the "Patients and Methods" section for a description of frequency, duration, and intensity scoring. Ellipses indicate not applicable.

† Baseline measured week before treatment start; change is last 7 days of treatment minus baseline.

‡ P (X < Y) indicates the Mann-Whitney statistic (reference measure for superiority).

§ CI indicates confidence interval; LB, lower boundary.

|| Generalized multiple Mann-Whitney test (stochastic ordering).

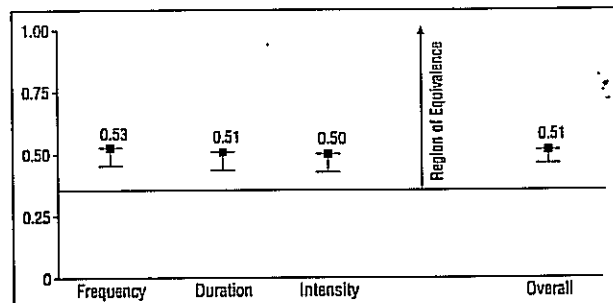


Figure 2. Equivalence or superiority in change from baseline for vertigo attacks. Data shown are Mann-Whitney statistics. Error bars indicate lower boundaries of 90% confidence intervals; solid line, upper bound of inferiority.

Mean relevant changes from baseline were not observed in either treatment group, neither for the clinical laboratory variables nor for the vital signs variables. There were no striking differences between the global tolerability assessments of the investigators and the patients or between the treatment groups (Mann-Whitney test, 2-sided: investigators, $P = .46$; patients, $P = .18$). For more than 90% of the patients, a good or excellent tolerability of the homeopathic remedy or betahistine was reported by the investigators.

COMMENT

Clinical evaluation of the efficacy of vertigo treatment is difficult. It requires the use of both objective criteria, such as frequency and duration of attacks and evidence of vestibular dysfunction, and subjective criteria, such as severity of vertigo, unsteadiness between attacks, cochlear symptoms, and vegetative symptoms. One of the main problems in the evaluation of any treatment is that the symptoms of

vertigo have 2 common features: discontinuity and variability in intensity.^{19,20} In the present clinical trial, all of these criteria were assessed. Subjective criteria must be given emphasis, since they reflect the patient's experience of discomfort. In this study, the homeopathic remedy proved to be as effective as betahistine in the treatment of vertigo of various origins. Concerning the associated symptoms, there was no statistically significant difference between the 2 treatment groups, whatever the population tested; this demonstrates therapeutic equivalence.

All clinical trials have shortcomings. In the present study, the exact cause of vertigo was unknown in 90% of the patients. However, for more than 70% of the patients in both treatment groups, none had been treated before. In general, in this early stage of a disease, no specific differential diagnosis is given, so that one third of patients of the homeopathic group were characterized as having vasomotor vertigo. Another shortcoming of this study was the lack of a placebo control. Although there are methodological reasons for a placebo control, the ethics of not treating a serious disease like vertigo must be considered. For this study, ethical considerations outweighed the methodological ideal. Furthermore, the efficacy of betahistine in the treatment of vertigo has been demonstrated in placebo-controlled studies and is accepted as a standard treatment for patients suffering from vertigo.^{11,12} Because of the taste differences between betahistine and the homeopathic remedy, a "double-dummy" design was used. This design guaranteed a high degree of blinding. Because of the lack of a placebo arm, the rate of spontaneous improvement in this trial is unknown, a common problem in clinical research. To reduce the rate of spontaneous improvement to a minimum, patients with less than 3 vertigo attacks during the week before the study began and with an intensity score

Table 3. Vertigo-Specific Questionnaire for the Evaluable Efficacy Sample*

Statistics†	Set 1‡			Set 2‡			Set 3‡			Set 4‡		
	Baseline	Change (Visit 2)§	Change (Visit 6)§	Baseline	Change (Visit 2)§	Change (Visit 6)§	Baseline	Change (Visit 2)§	Change (Visit 6)§	Baseline	Change (Visit 2)§	Change (Visit 6)§
Homeopathic group												
Patients, No.	52.0	52.0	51.0	53.0	53.0	52.0	53.0	53.0	52.0	53.0	53.0	52.0
Score												
Mean	58.5	+7.6	+28.6	53.6	+4.6	+29.2	65.2	+3.6	+19.0	47.9	+2.4	+11.8
SD	18.2	13.2	17.2	24.2	13.1	23.6	17.2	9.8	11.3	13.5	6.8	8.9
Median	58.9	+3.6	+28.6	56.3	0.0	+25.0	67.1	+2.6	+16.5	47.4	+1.3	+11.2
Betahistine group												
Patients, No.	52.0	52.0	52.0	52.0	52.0	52.0	52.0	52.0	52.0	52.0	52.0	52.0
Score												
Mean	64.6	+8.6	+25.8	58.4	+6.1	+28.7	72.8	+5.5	+16.8	49.7	+4.8	+12.5
SD	18.2	14.6	22.8	23.8	17.5	24.9	13.8	8.5	13.5	12.8	7.4	13.2
Median	64.3	+3.6	+25.0	56.3	+3.2	+25.0	72.4	+2.6	+17.1	52.6	+3.3	+9.9
P, Mann-Whitney test	.11300446
P (X<Y)	0.41	0.50	0.53	0.44	0.49	0.50	0.38	0.44	0.54	0.46	0.41	0.51
95% CI, LB	0.30	0.41	0.44	0.33	0.40	0.41	0.27	0.35	0.45	0.35	0.32	0.42
95% CI, UB	0.52	0.55	0.49	0.57

*Summary score of questionnaire transformed to a scale from 0 to 100, where 0 = maximum of symptoms and 100 = no symptoms. Plus signs emphasize the improvement. CI indicates confidence interval; LB, lower boundary; UB, upper boundary; and ellipses, data not applicable.
 †Set 1 assessed direct vertigo symptoms; set 2, intensity of vertigo during special exercises; set 3, vertigo-associated symptoms; and set 4, restrictions in daily life activities. See the "Patients and Methods" section for further descriptions of the 4 sets.
 ‡P (X<Y) is the Mann-Whitney statistic (reference measure for superiority).
 §Baseline measured week before treatment start, change (visit 2) after 3 days, and change (visit 6) after 42 days minus baseline.

Table 4. Summary Scores for the Quality-of-Life Questionnaires in the Evaluable Efficacy Sample*

Statistics†	Physical Health								Mental Health																
	Physical Functioning				Role Limitations Attributed to Physical Problems				Vitality				Role Limitations Attributed to Emotional Problems				Social Functioning				Mental Health				
	Baseline		Change		Baseline		Change		Baseline		Change		Baseline		Change		Baseline		Change		Baseline		Change		
	Baseline	Change	Baseline	Change	Baseline	Change	Baseline	Change	Baseline	Change	Baseline	Change	Baseline	Change	Baseline	Change	Baseline	Change	Baseline	Change	Baseline	Change	Baseline	Change	
Homeopathic remedy group																									
Patients, No.	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0
Summary scores																									
Mean	60.8	+18.7	42.2	+27.0	65.9	+7.1	52.2	+6.6	41.7	+9.1	49.0	+30.7	64.2	+8.6	52.8	+6.4									
SD	24.7	25.4	40.2	43.0	30.5	26.3	17.9	16.5	16.4	16.9	42.9	45.1	23.3	21.3	20.8	16.6									
Median	60.0	+15.0	25.0	+25.0	62.0	0.0	52.0	+5.0	40.0	+10.0	66.7	0.0	62.5	0.0	48.0	+4.0									
Betahistine group																									
Patients, No.	51.0	51.0	50.0	50.0	51.0	51.0	51.0	50.0	51.0	51.0	50.0	50.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0	51.0
Summary scores																									
Mean	64.8	+16.9	43.5	+24.5	68.5	+13.9	50.7	+11.5	44.6	+11.7	57.3	+22.7	67.4	+14.2	55.9	+8.5									
SD	27.1	29.5	41.0	44.2	29.2	28.8	19.0	19.7	14.4	16.1	43.2	48.3	23.9	20.8	16.6	16.1									
Median	65.0	+10.0	25.0	+12.5	72.0	0.0	45.0	+10.0	40.0	+10.0	66.7	0.0	62.5	+12.5	52.0	+4.0									
P, Mann-Whitney test	.3190684523284937	...									
P (X<Y)	0.44	0.55	0.49	0.52	0.48	0.42	0.54	0.44	0.43	0.45	0.44	0.54	0.46	0.43	0.45	0.46									
95% CI, LB	0.33	0.46	0.38	0.43	0.37	0.33	0.43	0.35	0.32	0.36	0.33	0.15	0.35	0.34	0.34	0.37									
95% CI, UB	0.55	...	0.60	...	0.58	...	0.65	...	0.54	...	0.55	...	0.57	...	0.56	...									

*Summary scores of the Medical Outcome Study-Short Form 36 questionnaires transformed to a scale of 0 to 100, with 0 = lowest possible quality of life and 100 = highest possible quality of life. Plus signs emphasize the improvement. Baseline measures week before treatment start; change is last 7 days of treatment minus baseline. CI, confidence interval; LB, lower boundary; UB, upper boundary; and ellipses, data not applicable.
 †P (X<Y) indicates the Mann-Whitney statistic (reference measure for superiority).

lower than 2 (on a 5-point rating scale) were excluded from the study.

The patient's global impression is an important variable to assess the efficacy of antivertigo medication. Many rating scales²¹ have been developed in an attempt to measure the specific influence of a disease on a patient's quality of life. A major general criticism of these instruments is that they were all developed in an attempt to provide a universal formula for evaluating the deterioration in enjoyment of life caused by a wide variety of disease processes. But some of them²² were specifically developed to determine the deterioration in quality of life induced by a specific disease syndrome. Besides the specific vertigo questionnaire, the validated and widely used quality-of-life questionnaire Medical Outcome Study-Short Form 36 was used as a secondary variable.¹⁴ Both treatment groups revealed slight superiorities or inferiorities for single groups of questions. But, in total, the outcome was similar. Prominent were the resultant comfort or sense of well-being of the patients; the extent to which they were able to maintain reasonable physical, emotional, and intellectual function; and the degree to which they retained their ability to participate in valued activities with family, in the workplace, and in the community.

All antivertigo medications have adverse effects, depending on their particular pharmacodynamic properties.² Therefore, their efficacy depends on the delicate balance between the benefits they impart in reducing the vertigo attacks and their unwanted effects. The tolerability of the homeopathic remedy and betahistine during this study was assessed as very good. Overall, it can be stated that, with the data obtained, the efficacy and safety of the homeopathic remedy in the treatment of vertigo of various origins was provable within the framework of a phase 4 clinical study.

CONCLUSIONS

The effectiveness and tolerability of a homeopathic remedy was compared with that of betahistine via a controlled double-blind study. Betahistine is considered a standard treatment for patients suffering from vertigo of various origins. Its efficacy has been reported in previous placebo-controlled studies. The study confirmed the therapeutic value of both treatments in patients suffering from vertigo of various origins as shown in the reduction of the frequency, intensity, and duration of vertigo attacks. Vertigo-specific complaints were significantly and similarly reduced in both treatment groups. The characteristics (improvement) of the quality of life, in combination with the statistically significant reduction of the vertigo attacks, are of clinical relevance. The tolerability of the homeopathic remedy and betahistine during the study was very good.

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