Efficacy of Betahistine by Patient-Reported Outcomes and its Tolerability Profile in Indian Patients with Vestibular Vertigo

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Abstract

Objective: Patients with vestibular vertigo suffer from disabling symptoms which affect their quality of life. This article presents the efficacy and safety profile of betahistine hydrochloride in Indian patients suffering from vestibular vertigo (OSVaLD study).

Methods: Study included patients suffering from vertigo, who were prescribed betahistine (48 mg/day) according to local label. Safety and efficacy populations of this study included 80 and 75 subjects respectively. The study included three visits: an initial baseline visit, and two follow-up visits (one month and three months [final visit] post-commencement of betahistine therapy). Efficacy was assessed by administering three patient-reported outcomes (PROs) namely, Dizziness Handicap Inventory (DHI), Hospital Anxiety and Depression Scale (HADS), and Medical Outcome Study Short Form-36 version2 (SF-36v2). Safety assessment was made by reports of Suspected Adverse Drug Reactions (SADRs) which began during the study.

Results: Mean changes in total DHI score for Indian efficacy population at follow-up and final visits were 31 and 44 points respectively. These changes indicated significant improvements in self-perceived impairment associated with vertigo. Similar improvements in quality of life were observed by HADS subscales (HADS-A and HADS-D) and SF-36v2 summary scores (PCS [physical component summary] and MCS [mental component summary]). There was only one report of SADR in this study in a female subject receiving betahistine 16 mg t.i.d. This SADR was gastritis of mild severity and was probably not related to betahistine.

Conclusion: A significant number of vestibular vertigo patients reported fair degree of spontaneous recovery. Betahistine treatment improved quality of life, was safe and well-tolerated by Indian patients suffering from vertigo.

Introduction

Vertigo is an illusion of movement (mostly spinning) caused due to imbalance of the vestibular system. In spite of being a common symptom associated with varying underlying diseases, there are very few reports in literature about prevalence of vertigo in India.¹,² Vertigo significantly impairs general health status and quality of life in patients with vestibular disorders.³⁴ Therefore quality of life instruments may be used as an important tool to determine efficacy of different treatment options.

Betahistine is commonly used in the management of vestibular disorders. Several studies have demonstrated efficacy of betahistine in comparison with placebo and different anti-vertigo drugs⁵⁻¹⁰ but its impact on health related quality of life (HRQoL) has been rarely investigated.⁷,⁸ Thus, with the central objective of obtaining real world data about efficacy profile of betahistine using patient related outcomes (PROs), an international study, OSVaLD, (A Three-Month Observational Study in Patients Suffering from Recurrent Peripheral Vestibular Vertigo to Assess the Effect of Betahistine 48 mg/day on Quality of Life and Dizziness Symptoms) was conducted. Three instruments: Dizziness Handicap Inventory...
(DHI), Hospital Anxiety and Depression Scale (HADS), and Medical Outcome Study Short Form-36 version 2 (SF-36v2) were used in this study. Final primary findings from OSVaLD, and initial baseline data including an extensive by-country analysis from this study have been reported in individual publications. The present article presents the efficacy and safety of betahistine under routine clinical practice in Indian geographical and ethno-cultural conditions.

Methods

Study design

OSVaLD was an international, multicenter, open-label, study of betahistine under real-life conditions in patients with vertigo of peripheral vestibular origin. The study was carried out as a world-wide programme across 13 countries between April, 2005 and October, 2006. The data reported in this article was collected across 23 centers located in India.

Betahistine 48 mg/day (24 mg tablet b.i.d. or 16 mg tablet t.i.d) was initiated as monotherapy or as an adjuvant therapy when the current anti-vertigo therapy was not sufficient or tolerated. Prior or concomitant medications could be used as needed.

The study included three clinic visits: an initial baseline visit to the treating physician, one follow-up visit (one month post-commencement with betahistine therapy), and a final evaluation visit (at three months post-commencement with betahistine therapy or early termination of betahistine). This study schedule was matched with the treating physician’s usual consultation pattern.

Subjects

The study included patients who were being prescribed betahistine according to local labeling, and who had history of vertigo attacks of peripheral vestibular origin not exceeding 5 years, with baseline total Dizziness Handicap Inventory (DHI) score ≥40. Patients who had contraindications to betahistine as described by local labeling were excluded from the study.

Efficacy and safety assessments

The study used three well-established PRO instruments, namely DHI, HADS, and SF-36v2 to evaluate effect of betahistine on dizziness symptoms, symptoms of anxiety and depression, and quality of life, respectively, in patients with peripheral vestibular vertigo. These instruments were administered on scheduled study visits.

The primary outcome measure of the study was to determine the effect of betahistine on dizziness, measured as change in total DHI score at 3 months from baseline. DHI is a self-report questionnaire used to assess the degree of disability associated with dizziness regardless of its underlying cause(s). It consists of 25 items (questions) covering three subscales with functional (9 items), emotional (9 items) and physical (7 items) aspects. “Yes” scores 4 points, “sometimes” 2 points and “no” 0 points. Total DHI-score ranges from 0 to 100. Maximum scores for functional, emotional and physical aspects are 36, 36, and 28 respectively. Higher scores indicate greater perceived disability.

HADS is a self-report scale used to measure anxiety and depression symptoms. It consists of 14 items covering two mood subscales: HADS-A (contains 7 items for anxiety) and HADS-D (contains 7 items for depression). Each item is rated on a four-point scale (scored 0-3), giving maximum scores of 21 for each of these subscales. HADS-A and HADS-D are interpreted as follows: 0-7 points = normal, 8-10 points = mild, 11-14 points = moderate, and 15-21 = severe.

For DHI and HADS, if at least 50% of items were complete in the subscale, the missing values were assumed as equal to the mean of subscale. Otherwise the subscales and scale scores were not calculated.

SF-36v2 is a widely used generic instrument for measurement of health-related quality of life (HRQoL). It contains 8 scales and 2 summary scales based on 36 items which measure physical and mental health status. These scales are: physical functioning (PF), role limitations due to physical health (RP), bodily pain (BP), general health perceptions (GH), vitality (VT), social functioning (SF), role limitations due to emotional problems (RE), and mental health (MH). Scores from these scales can be combined into physical and mental component summary (PCS and MCS). Responses to each item were scored and summed to yield scale and summary scores from 0 to 100. Higher scores represent better self-perceived health. Instead of using original scores ranging from 0 to 100, norm-based scoring results were used. Data were scored in relation to the 1998 U.S. general population norms. Using norm-based scoring method, easier and meaningful interpretation of scale and summary scores can be made.

All scores above or below 50 can be interpreted as above or below the general population norms. Standard deviations are equalized at 10, therefore it is easy to see exactly how far above or below the average score any result is in standard deviation units. The rules of scoring were as per SF Health Outcomes Scoring Software of Quality Metric Incorporated. An important rule for scoring was that an incomplete scale score may be estimated if answers exist for at least 50% of the items within that scale. The average score of the completed items replaces any missing responses within the scale.

At the end of the study, patient’s and investigator’s impression of the treatment was assessed as “excellent”, “good”, “moderate”, etc.
Table 1: Baseline demographic characteristics of patient populations

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Efficacy population (N = 75)</th>
<th>Safety population (N = 80)</th>
</tr>
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<tbody>
<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>73 (100)</td>
<td>78 (100)</td>
</tr>
<tr>
<td>Age (years)†</td>
<td>45.4 ± 14.5</td>
<td>45.3 ± 14.1</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>36 (48)</td>
<td>38 (47.5)</td>
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<tr>
<td>Age (class [years]), n (%)‡§</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-29</td>
<td>8 (11)</td>
<td>8 (10.3)</td>
</tr>
<tr>
<td>30-39</td>
<td>23 (31.5)</td>
<td>24 (30.8)</td>
</tr>
<tr>
<td>40-49</td>
<td>14 (19.2)</td>
<td>17 (21.8)</td>
</tr>
<tr>
<td>50-59</td>
<td>15 (20.5)</td>
<td>16 (20.5)</td>
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<tr>
<td>60-69</td>
<td>11 (15.1)</td>
<td>11 (14.1)</td>
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<tr>
<td>70-79</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>80-89</td>
<td>1 (1.4)</td>
<td>1 (1.3)</td>
</tr>
<tr>
<td>≥90</td>
<td>1 (1.4)</td>
<td>1 (1.3)</td>
</tr>
<tr>
<td>Height (cm)‡§</td>
<td>163 ± 11</td>
<td>163 ± 11</td>
</tr>
<tr>
<td>Weight (kg)‡‡</td>
<td>63.9 ± 10</td>
<td>64.0 ± 9.9</td>
</tr>
<tr>
<td>BMI (kg/m²)¶</td>
<td>24.4 ± 4.2</td>
<td>24.3 ± 4.1</td>
</tr>
</tbody>
</table>

*Calculation based on data from 73 patients in the efficacy population; †Calculation based on data from 78 patients in the safety population; ‡Calculation based on data from 65 patients in the efficacy population; §Calculation based on data from 70 patients in the safety population; ¶Calculation based on data from 74 patients in the efficacy population; ‖Calculation based on data from 65 patients in the safety population.

and “poor” and scored with 1, 2, 3, and 4 points respectively.

For safety assessments reports of suspected adverse drug reactions (SADRs) were obtained during month 1 and month 3 visits.

Statistical considerations

Based on results of previous studies conducted on betahistine, OSVaLD study targeted 200 patients per country for robust results. The efficacy population included all subjects allocated to treatment who received a prescription of betahistine at baseline, and (i) who had at least one subsequent clinic visit (follow-up visit, final visit or endpoint visit), (ii) who had a score calculated for at least one of the three outcome scales (DHI total, SF-36v2 [both summary scores] or HADS [both anxiety and depression scales]) at the baseline visit or at least one post-baseline visit. Scores on each of the three scales (and scores on the different subscales) were summarized by descriptive statistics by visit including last visit on-treatment. Changes from baseline for all efficacy parameters were presented by descriptive statistics, including 95% confidence intervals and one-sample t-test. Analyses were done on efficacy population as a whole, as well as for subgroups based on gender, disease (baseline cause of vertigo) and betahistine monotherapy vs. combination therapy.

Safety was assessed in the safety population that included all subjects allocated to treatment who received a prescription of betahistine at baseline, and who had at least one subsequent clinic visit.

Exposure was described by total treatment duration. Safety was assessed by reports of SADRs which began during the study. All SADRs were coded according to Medical Dictionary of Regulatory Activities (MedDRA) classification version 9.0 (presentation of primary SOC [System Organ Class], HLT [High Level Term] and PT [Preferred Term]) and were presented in summary tables, with number and percentage of subjects who reported that SADR by preferred term. These SADRs were also presented according to their severity and their relationship to the study drug as judged by the investigator.

Study conduct and organization

The study was conducted according to International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Harmonized Tripartite Guideline for Good Clinical Practice (GCP), and Declaration of Helsinki and its subsequent revisions. The protocol and informed consent were approved by the ethics committee at each center prior to study initiation as per national regulatory requirements. Investigator(s) in this study were general practitioners and specialists.

Data management and statistical analysis were conducted by the FOVEA Group, Rueil Malmaison, France. Data entry was performed using Access version 9.0. Quality control was performed using SAS version 8.2. Statistical analysis was performed using SAS version 8.2 and SF Health Outcomes™ Scoring Software of Quality Metric Incorporated (Enhanced module + utility index).

Results

OSVaLD study included 2168 subjects, of which 2032 and 1898 were included in safety and efficacy populations respectively. In India, 100 patients were included in this study, of which safety population consisted of 80 subjects and efficacy population included 75 subjects. Baseline demographic characteristics of these populations are presented in Table 1. As can be seen from Table 1, there were no substantial differences in baseline demographic characteristics of efficacy and safety populations.

There were almost equal proportions of males and females (52% and 48% respectively) in efficacy population. Subjects in Indian efficacy population were prescribed betahistine predominantly because of Ménière’s disease (34.7% cases) followed by benign paroxysmal positional vertigo (BPPV, 29.3% cases) and peripheral vestibular vertigo of unknown pathophysiology (16% cases). This was in contrast to overall OSVaLD efficacy population wherein peripheral vestibular vertigo of unknown pathophysiology was the predominant cause (38.4% cases), followed by BPPV (22% cases), and Ménière’s disease (13.9% cases) (Figure 1).

Principal reasons for a prescription of betahistine were new diagnosis (65.3% cases), insufficient efficacy of current therapy (30.7% cases), and inability to tolerate other...
medications (4% cases). Betahistine was prescribed as monotherapy and in combination with other therapies for vertigo in 57.3% and 42.7% cases respectively. Almost equal proportions of patients were prescribed betahistine 24 mg b.i.d. (52% cases) or 16 mg t.i.d. (48% cases).

**Efficacy outcomes**

**DHI**

The mean baseline values for the physical, emotional, functional, and total scores were 19.6 ± 5.4, 17.9 ± 6.6, and 24.0 ± 5.2, and 61.6 ± 11.8 respectively. Statistically significant decrease (p <0.0001 vs. baseline) was observed in all these indices at follow-up and final evaluation visits (Figure 2). The mean values for physical, emotional, functional, and total scores improved to 6.8 ± 5.6, 4.1 ± 5.9, 6.7 ± 6.4, and 17.6 ± 16.1 respectively at final evaluation visit.

Mean changes from baseline in DHI response scores at the follow-up visit and final evaluation visit were statistically significant (p <0.0001) regardless of gender, however mean change in total score was numerically greater in males as compared to females. Subgroups of patients with vertigo due to Ménière’s disease and benign paroxysmal positional vertigo (BPPV) showed statistically significant improvements at the follow-up and final evaluation visits (p <0.0001 vs. baseline). Mean changes from baseline in DHI response scores of subgroups receiving betahistine as monotherapy, or as combination with other therapies were also statistically significant at the follow-up visit and final evaluation visit (p <0.0001).

**HADS**

Mean baseline HADS-A score of efficacy population was 10.0 ± 4.9; 31.9% (23/72) patients had normal anxiety level, 30.6% (22/72) patients had moderate anxiety level, 23.6% (17/72) had mild anxiety level, and 13.9% (10/72) patients had severe anxiety level (Fig. 3). Proportion of patients having severe anxiety was lower among Indian efficacy population compared to overall OSVaLD efficacy population (15.9% [296/1858]). Proportion of patients with normal anxiety level increased from 31.9% (23/72) at baseline to 66.2% (47/71) at the follow-up visit, and to 82.8% (53/64) at the final visit (Figure 3). Higher proportion of males (86.5% [32/37]) had normal anxiety level compared to females (77.8% [21/27]) at final visit.

Mean baseline HADS-D score was 8.4 ± 5.2; 40.3% (29/72) patients had normal depression level, 29.2% (21/72) patients had mild depression level, 22.2% (16/72) had moderate depression level, and 8.3% (6/72) patients had severe depression level. Proportion of patients having severe depression was numerically lower among Indian efficacy population compared to overall OSVaLD efficacy population (9.3% [17/1898]).

![Fig. 1: Baseline qualifying diagnosis of efficacy population in the overall OSVaLD study, and Indian subset stratified by identity of enrolling physician](image1.png)

![Fig. 2: Mean changes from baseline in total dizziness handicap inventory (DHI) score and subscale scores in the Indian efficacy population](image2.png)
Changes from baseline at final visit in HADS-A and HADS-D scores were statistically significant ($p < 0.0001$) in efficacy population (Figure 3) and across subgroups based on gender, and monotherapy vs. combination therapy.

**SF-36®v2**

At the baseline visit, the mean PCS and MCS scores were 42.5 ± 8.0 and 34.6 ± 12.4 respectively. These scores were below the U.S. general population norm, indicating a reduced HRQoL status. Change from baseline at follow-up and final evaluation visits in both PCS and MCS scores were statistically significant ($p < 0.0001$) (Figure 4). Improvements in PCS and MCS at final visit from baseline were statistically significant across subgroups based on gender (Table 2), and monotherapy vs. combination therapy. Changes observed in Indian efficacy population were numerically higher as compared to total OSVaLD efficacy population (Table 2).

### Overall efficacy assessment

The impression of treatment was excellent for 44.6% (29/65) subjects, good for 49.2% (32/65) subjects, and moderate for 6.2% (4/65) subjects. None of the patients assessed the treatment as poor. Proportion of subjects who assessed the treatment as excellent was higher in Indian efficacy population compared to overall OSVaLD efficacy population (44.6% vs. 36.6%). Indian efficacy population, higher proportion of females in rated the treatment as excellent compared to males, and higher proportion of males rated the treatment as good compared to females. When items “excellent”, “good”, “moderate”, and “poor” were scored with 1, 2, 3, and 4 points, the mean score for subject’s impression of the treatment was determined to be 1.6 ± 0.6.

The investigators’ impression of the treatment was excellent for 36.9% (24/65) subjects, good for 56.9% (37/65), and moderate for 6.2% (4/65) patients. Treatment of none of the patient was found to be poor. The investigator’s impression of the treatment was 1.7 ± 0.6 (mean ± SD). Statistically significant correlation existed between physician’s opinion and subject’s opinion ($r = 0.63, p < 0.0001$).

Subgroup analysis of subject’s and investigator’s impression scores indicated similarity regardless of gender. Subject’s and investigator’s impression scores were numerically higher for peripheral vestibular vertigo of unknown pathophysiology and Ménière’s
The efficacy of betahistine.7-8 have utilized PROs for assessing few studies are reported which to the best of our knowledge, only incapacities influencing daily life. However, data suggests that 40-70% of patients with migraine related vertigo have positional vertigo in the course of the disease which is not benign positional vertigo.19 During the completion of this study, published epidemiological data regarding the high prevalence about migraine related vertigo was not available; hence there is a high possibility that many cases of recurrent vertigo were actually migraine related vertigo but were diagnosed otherwise. Further, the improvement in these patients also opens a new possibility that betahistine therapy may be beneficial in this class of patients.

### Table 2: HRQoL status as determined by SF-36®v2 in efficacy population

<table>
<thead>
<tr>
<th>SF-36®v2 scale (PCS and MCS)</th>
<th>Male (N = 39)</th>
<th>Female (N = 36)</th>
<th>Efficacy population (India) (N = 75)</th>
<th>Efficacy population (N = 1898)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At baseline visit</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCS</td>
<td>45.0 ± 8.6</td>
<td>40.0 ± 6.7</td>
<td>42.5 ± 8.0</td>
<td>39.8 ± 7.9</td>
</tr>
<tr>
<td>MCS</td>
<td>33.8 ± 12.8</td>
<td>35.4 ± 12.2</td>
<td>34.6 ± 12.4</td>
<td>35.5 ± 11.5</td>
</tr>
<tr>
<td>At final evaluation visit*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCS change from baseline</td>
<td>7.7 ± 8.8</td>
<td>11.6 ± 8.0</td>
<td>9.5 ± 8.6</td>
<td>7.8 ± 8.8</td>
</tr>
<tr>
<td>MCS change from baseline</td>
<td>18.4 ± 16.3</td>
<td>14.9 ± 15.2</td>
<td>16.8 ± 15.8</td>
<td>10.8 ± 12.7</td>
</tr>
</tbody>
</table>

All values: Mean±SD; *p (intra-group)<0.0001; HRQoL = Health related quality of life, MCS = Mental Component Summary, PCS = Physical Component Summary, SD = Standard Deviation, SF-36®v2 = Short-Form 36 Health Survey Version 2.

Safety outcomes

The mean betahistine treatment duration was 93.8 ± 42.5 days.

Only one SADR was reported from India in a female subject receiving betahistine 16 mg t.i.d. This SADR was gastritis of mild severity, and was judged to be probably related to betahistine.

Discussion

Efficacy and tolerability of betahistine for the treatment of peripheral vestibular vertigo is supported by various clinical studies reported previously.5-10 In most of these studies efficacy of betahistine has been established by evaluating its effect on frequency, duration, and severity of vertigo attacks. Another method which has been less utilized to assess the treatment outcome is use of PROs before and after treatment. This becomes particularly important for conditions like vertigo which is accompanied by incapacities influencing daily life. However, to the best of our knowledge, only few studies are reported which have utilized PROs for assessing the efficacy of betahistine.7,8

OSVaLD study provided a unique opportunity to capture extensive real-world data of effect of betahistine on HRQoL of a large patient population across 13 countries. The study used both disease-specific as well as generic instruments for efficacy assessments. Overall results of OSVaLD study have been published previously by Benecke et. al.11 The results presented in present article provide a deeper insight to efficacy and safety of betahistine in Indian population. A substantial proportion of Indian efficacy population was with peripheral vestibular vertigo of unknown pathophysiology (16%). Although this proportion was lower in comparison with the overall OSVaLD efficacy population (38.4%), yet it was much higher in comparison to other reports wherein diagnosis for vertigo could not be specified only for 1.5% patients.17 Etiological diagnosis in vertigo patients is possible only through collection of detailed medical history and performing clinical examinations, which is quite a time consuming procedure. Moreover, for performing the clinical neurootological and vestibular function tests, sophisticated investigations such as Videonystagmography [VNG], Electronystagmogram [ENG], Video Head Impulse Test [VHIT], Subjective Visual Vertical [SVV], Posturography, and ECOG [Electrocochleography]) are required. The present study was conducted in busy OPD settings, where physicians were unable to collect the detailed medical history and at most places infrastructure required for performing necessary investigations was not available, therefore a substantial proportion of efficacy population was with peripheral vestibular vertigo of unknown pathophysiology.

It is to be noted that at the time of conduct of this study, the qualifying diagnosis for patient population included BPPV; however recent guideline intended for diagnoses and management of BPPV do not recommend the routine treatment of BPPV with vestibular suppressant medications such as antihistamines.18 Data suggests that 40-70% of patients with migraine related vertigo have positional vertigo in the course of the disease which is not benign positional vertigo.19 During the completion of this study, published epidemiological data regarding the high prevalence about migraine related vertigo was not available; hence there is a high possibility that many cases of recurrent vertigo were actually migraine related vertigo but were diagnosed otherwise. Further, the improvement in these patients also opens a new possibility that betahistine therapy may be beneficial in this class of patients.

DHI and its various adaptations have been used previously in several studies to investigate the severity of dizziness in various populations,3,20,21 and effect of treatments on dizziness of different etiologies.4,22,23 Dizziness can cause substantial impairment in patients; therefore the primary criterion evaluated was absolute change in mean total DHI score between three month visit and baseline. The baseline total DHI score of Indian efficacy population was approximately 62 which suggested severe functional impairment.24 Mean change in total DHI score at follow-up and final visits were approximately 31 and 44 points respectively. These improvements were substantially higher than threshold of 18 points which is known to be a significant change in patient’s self-perceived health.13 The improvements in individual health aspect (physical, emotional, and functional subscores) and in total scores at follow-up and final visits were statistically significant across subgroups based on gender and betahistine monotherapy vs.
combination therapy. Patients with baseline MD or BPPV (64% of efficacy population) also showed statistically significant improvement in DHI subscores and total score at follow-up and final visits. A comparison of results obtained from Indian population subset with other 13 countries participating in OSVaLD revealed that improvement in total DHI score was highest in India. Efficacy of betahistine as determined by DHI for overall OSVaLD population and Indian subset were in line with other studies reported previously.7,8

Very often vertigo patients deliberately impose limitations on their daily routine activities in order to avoid embarrassment, which may ultimately lead to co-morbid depression. Clinically relevant levels of depression have been indicated in vertigo patients.25 It has also been suggested that vertigo patients with abnormal depression feel more disabled than those without depression,26, 27 resulting in poor quality of life. All three instruments used in this study to evaluate quality of life in vertigo patients, i.e., disease specific (DHI) as well as general (HADS and SF-36®v2) included assessment of depression. Correlations between assessments made by DHI, HADS, and SF-36®v2 have been reported in several other studies.3,26 In our study, improvements recorded by generic instruments after completion of betahistine treatment are indicative of poor HRQoL caused by vertigo, though the contribution of non-vertigo factors to these scores cannot be ignored.

Betahistine was found to be safe and tolerable because there was only one incidence of SADR reported in the Indian safety population. The target population-pool of 200 subjects per country could not be achieved in India but the results obtained for efficacy parameters are statistically significant and consistent with results obtained for overall OSVaLD population and other participating countries. This suggests that results presented in this article are true indicator of efficacy and safety of betahistine.

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References