

## EFFECTS OF DIURETIC AND VASODILATOR THERAPY IN MENIERE'S DISEASE

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### ABSTRACT

*Introduction: Meniere's disease is recognised by frequent periods of remissions. The available wisdom about the disease and treatment reflects the opinion of experienced clinicians, rather than scientific facts.*

*Objective: To determine the efficacy of vasodilator and diuretic therapies in the prophylaxis of Meniere's disease. A randomized controlled trial. The study was carried in the ENT Department, Combined Military Hospital, March 2007 to Dec 2009.*

*Subjects and Methods: All new patients (N = 120) of clinically diagnosed Meniere's disease were included by consecutive non-probability sampling. Demographic characteristics of the patients were noted and the patients were divided into three groups irrespective of age and sex. Group A was placed on amiloride 5 mg and hydrochlorothiazide 50 mg combination, one tablet daily, the Group B on tablet betahistine hydrochloride 48 milligram in three divided doses and Group C patients on tab multivitamin once daily respectively. The patients were reviewed after 06 weeks.*

*Results: Improvement in vertigo was seen in 77% in group A, in 68% patients in group B and in 45% in group C (p = 0.021). Hearing thresholds improved in 54% in group A, 63% in group B and in 36% in group C (p = 0.067). There was subjective improvement in tinnitus in 54% in group A, 80% in group B and in 37% in group C. Diuretic and vasodilator had a definitive and significant effect in Meniere's disease, in controlling vertigo and tinnitus, when compared with placebo (p < 0.05).*

*Conclusion: Diuretics and vasodilators do have a significant role in the prophylaxis of Meniere's disease.*

*Keywords: Meniere's disease, endolymphatic hydrops, vertigo, hearing loss, tinnitus, diuretic therapy, vasodilator therapy.*

### INTRODUCTION

Meniere's disease remains, in many ways, as much an enigma as it was when Prosper Meniere reported patient with episodic vertigo attacks in 1861.<sup>1-3</sup> The illness has frequent periods of remission, and only subjective reports of efficacy exist for most treatments.<sup>4</sup> Needless to say much of conventional wisdom regarding Meniere's disease merely reflects the opinion of experienced clinicians, rather than scientific fact. The medical literature on this disease has become vast and continues to grow.<sup>5,6</sup> However, the amount of proven scientific knowledge is embarrassingly small, and many questions remain unanswered. Currently, the treatment of Meniere's disease is empirical.<sup>7</sup> Time spent in giving a complete explanation of the disorder and an outline of the anticipated course of the disease is therapeutic in itself and invariably has a positive effect on the subsequent management. Two commonly used drugs given for prophylaxis purpose in Meniere's disease are diuretics

and vasodilators. A lot of work has already been done regarding the prophylaxis of Meniere's disease but in Pakistan, literature on this subject is rather scanty.<sup>4</sup>

We have selected this topic with the aim to evaluate and compare the effects of diuretic, vasodilator therapies in Meniere's disease and also to compare these results with those mentioned in the literature so that a better regime of treatment can be formulated for the patients with Meniere's disease. To the best of our knowledge, no such study has been conducted in our population.

### SUBJECTS AND METHODS

*This randomised control trial was conducted in ENT Department, Combined Military Hospital Lahore, from March 2007 to Dec 2009. All new patients (N = 120) with clinically confirmed diagnosis of Meniere's disease were included in the study. The age ranged from 41 to 68 years (mean 50.5 ± 7.17);*

males to females ratio was 1; 1.17, 1:1.21, and 1: 1.11 in group A, B, and C respectively (Fig. 1, 2).

#### Minimum diagnostic criteria (inclusion criteria)

- Patients with history of typical triad of symptoms i.e. episodic vertigo (at least 2 definitive episodes of vertigo of at least 20 minutes duration), tinnitus and hearing loss (minimum hearing loss of 30 db in any of 500, 1000 and 2000 htz).

#### Exclusion criteria

The following patients were excluded from the study.

- Patients presenting with atypical features.
- Patients with tinnitus as major symptom and showing retro – cochlear deafness on audiometric testing.
- Patients with acute or chronic middle ear disease presenting with Meniere's like syndrome.
- Patients allergic to any of the two drugs were also excluded from the study.
- Patients with positive VDRL.

The project was approved by the hospital Ethics Committee and informed consent was taken from all the participants. The patients were randomly placed in three equal groups A, B and C. The treatment groups were comparable in terms of demographic features, age, gender, income level, marital status, ethnic origin and education level. The study was started one week after the acute episode of disease had settled.

Group A: was started with tablet Amiloride hydrochloride 5 mg, Hydrochlorothiazide 50 mg one tablet daily along with advice for salt restriction.

Group B: was advised Betahistine dihydrochloride 48mg in three divided doses.

Group C: The patients were given tablet multivitamin one daily.

The following instructions were given to the patients at the start of medication.

Patients were given a questionnaire / proforma, and advised to fill in following information (Proforma was translated when required in Urdu and was briefed how to fill it).

#### Vertigo:

Number of attacks

Severity of attacks

Mild (vertigo with no nausea; could perform routine work).

Moderate (vertigo with nausea; had to suspend work during the attack).

Severe: Vertigo +nausea + vomiting + had to stay in bed.

Both reduction in number and severity (alone or in combination) will be taken as improvement.

#### Tinnitus;

Mild (rated on VAS 1 – 3).

Moderate (rated on VAS 4 – 7).

Severe (rated on VAS 8 – 10).

#### Hearing loss:

Same as before

Worse.

Better.

All Patients were followed for a period of one year. Overall improvement was defined as improvement in vertigo with or without improvement in tinnitus and hearing loss. Improvement in vertigo meant decrease in number or severity of attacks or both. Improvement in tinnitus was defined as improvement of 2 or more points on VAS while improvement in hearing was defined as subjective feeling of improvement, confirmed on PTA (change of  $\geq 10$  dB in hearing threshold on better side was taken as improvement).

The results were analysed using the Statistical Package for the Social Sciences Version 16 and Chi Square test was applied to compare the effect of medication for vertigo, hearing loss and tinnitus. Significance was tested at p-value of 0.05; values less than 0.05 were considered significant ( $p < 0.05$ ).

## RESULTS

A total of 120 patients were selected with typical features of Meniere's disease. *Only 106 were left by the end of treatment as 14 patients were lost to follow-up.*

As far as vertigo is concerned, 27 patients of the 35 (77%) showed improvement in diuretic group whereas this improvement was 24 / 35 (68%) and 16 / 35 (45%) in vasodilator and placebo group respectively. This improvement was statistically significant ( $p = 0.021$ ). Hearing thresholds improved in 19 / 35 (54%) group A, 23 / 36 (63%) in group B and in 13 / 36 (36%) in group C. However the result was not statistically significant ( $p = 0.067$ ).

There was subjective improvement in tinnitus in 19 / 35 (54%) in group A, in 28 / 35 (80%) in group B and in 13 / 35 (37%) in group C. This too was statistically significant ( $p = 0.02$ ) (Fig. 3, 4, 5).

## DISCUSSION

The sense of balance is very basic and phylogenetically predates sight and hearing. Meniere's is not a rare disease and vertigo in peripheral vestibular lesion as in Meniere's disease is very alarming to the patient.

Presently the most commonly used medical interventions for prophylaxis purpose in Meniere's

disease are diuretic and vasodilators. Commonly used diuretics are thiazides which are often added with potassium sparing diuretics. Thiazide diuretics induce a diuresis by blocking sodium reabsorption in the proximal portion of distal tubule of the nephron. Amiloride blocks the epithelial sodium channel in the late distal convoluted tubules, connecting tubules, and collecting ducts in the kidneys thereby inhibiting sodium reabsorption. This promotes the loss of sodium and water from the body, but without depleting potassium. Regime of fluid and salt restricted diets along with a diuretic has long been recommended in the treatment of Meniere's disease.<sup>8</sup> In the vasodilator group, betahistine hydrochloride is the prototype drug. Betahistine releases histamine in the body, when taken by mouth, and

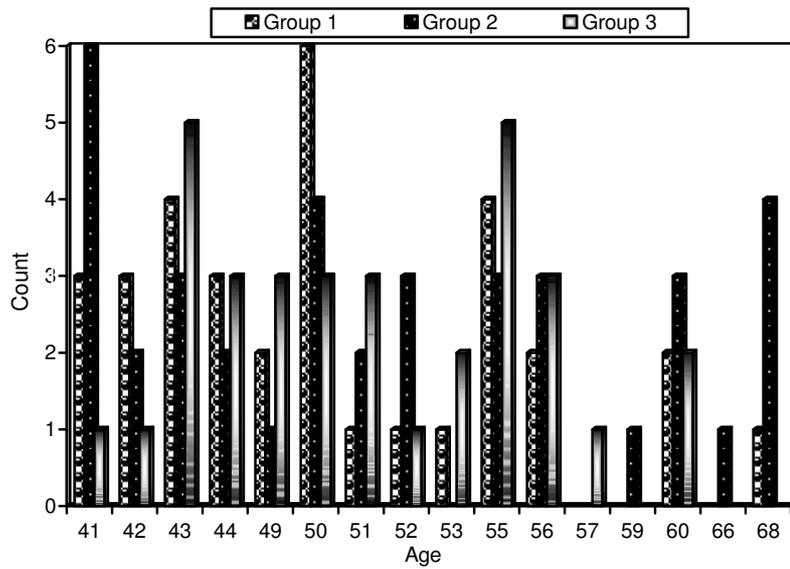


Fig. 1: Age Demographic characteristics.

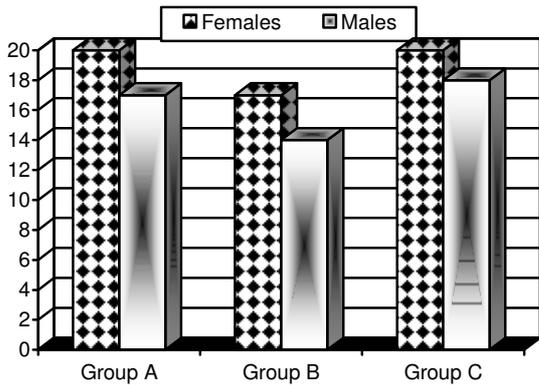


Fig. 2: Gender Distribution.

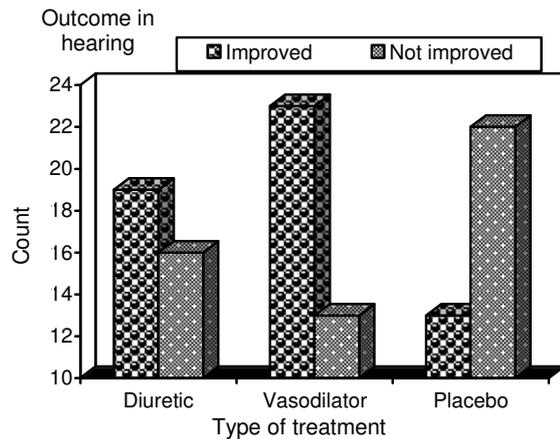


Fig. 4: Effect on Hearing.

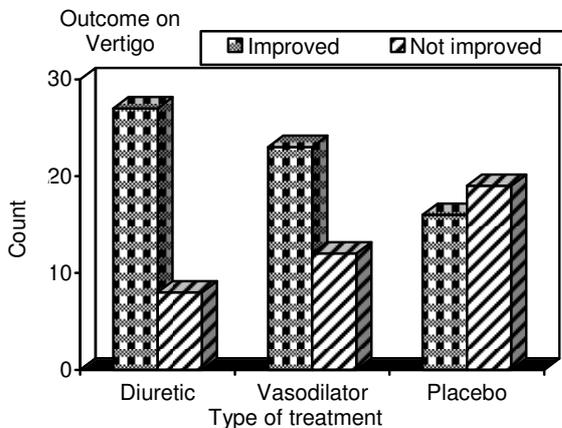


Fig. 3: Effect on Vertigo

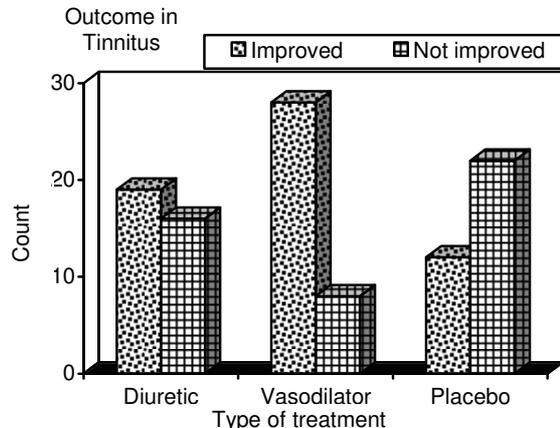


Fig. 5: Effect on Tinnitus:

has been shown to increase cochlear flow. It causes vasodilatation in the stria vascularis and lowers endolymph pressure.

Our study shows that diuretic therapy and vasodilator therapy have a considerable effect in the prophylaxis of Meniere's disease when compared to placebo. The response to diuretic was similar to the study conducted by Klockhoff and Lindblom.<sup>9</sup> In their trial, hydrochlorthiazide had a considerable effect in hearing, tinnitus, vertigo, and general condition over that obtained by placebo.<sup>9</sup> Another study by Klockhoff, Lindblom and Stahle also claimed to show a significant reduction in attacks of vertigo in long term study of chlorthalidone.<sup>10</sup> Vertigo, which is the most troublesome symptom of the disease, decreases in frequency, duration and intensity as well. Effect of diuretic therapy on hearing in Meniere's disease is also optimistic and the hearing loss can be prevented to worsen if the disease is diagnosed early and treatment started. However in a retrospective review by Corvera and Corvera, in a cross over placebo control study and Van Deelen and Huinzing it was advocated that diuretic therapy did have an effect on vertigo but did not prevent deterioration of hearing in Meniere's diseases.<sup>11 12</sup>

Vasodilator therapy also has analogous effect in controlling vertigo, hearing loss and tinnitus in Meniere's disease. Jackson, Glasscock et al retrospectively compared a group of patients treated with vasodilators to a subsequent group treated with diuretic.<sup>13</sup> This group did only marginally better with diuretics. In two double blind cross over trials by Frew and Menon, betahistine was advocated as important treatment modality in control of vertigo.<sup>14</sup> However, the study was limited by short duration. The clinical effectiveness of betahistine has also been demonstrated in recent years in a double – blind, randomized, placebo, and active controlled studies in a numbers of patients.<sup>15</sup> Hence vasodilator therapy can be well thought – out as a best possible substitute for diuretic therapy in Meniere's disease compared to placebo. In another study conducted by Redon et al, the recovery time was compared in 16 patients who received either a placebo or betahistine. Betahistine was found to be effective within 4 days after treatment administration, and the effect continued for whole of the treatment period (up to 3 months).<sup>16</sup> In one meta – analysis by Della, Guidetti and Eandi, the benefit of betahistine for the vertiginous symptomatology related to other vertiginous pathologies was ascertained.<sup>17</sup> Bertrand reported a long term evaluation of betahistine treatment in Meniere's disorder.<sup>18</sup> In this study of 60 patients treated for 12 to 14 years; 13 were symptom free at death or follow up, 36 required continuous treatments to avoid relapse and 11 were failures and had revision surgery. A review of the literature on drug therapy for Méni-

ère's disease was made by Claes and Heyning to search for all publications between January 1978 and September 1998. Only betahistine and diuretics appear to have proven efficacy in double – blind studies on the long term control of vertigo.<sup>19</sup>

## CONCLUSION

It is **concluded** that diuretics and vasodilators do have a role in the prophylaxis of Meniere's disease and definite improvement occurs after Diuretic and vasodilator therapy, at least in vertigo and tinnitus. Improvement in hearing is clinically significant though not statistically. However, more work is required for formulation of a definitive regime which can reverse or at least halt its progression.

## SUMMARY

*What is already known on the subject:*

- Meniere's disorder is not a rare disease. The medical literature on this disease has become vast and continues to grow. However, the amount of proven scientific knowledge is embarrassingly small, and many questions remain unanswered.
- Two commonly used drugs given for prophylaxis purpose in Meniere's disease are diuretics and vasodilators.

*What this Article has added to our understanding:*

- There is not a single study conducted locally to compare these commonly used therapeutic modalities. This study has shown the pharmacological effects of these commonly prescribed drugs in our population.

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