

Cetirizine and Astemizole in Allergic Rhinitis : A Comparative Study

R. K. Jain, Head, Department of E.N.T., Institute of Medical Sciences,
Banaras Hindu University, Varanasi - 221 005

Abstract

The efficacy, safety and side effects of Cetirizine and Astemizole were compared with Pheniramine maleate in sixty cases of allergic rhinitis. All medications were stopped one week prior to treatment. Cetirizine, Astemizole or Pheniramine maleate were given as a single daily dose for 15 days. On completion of treatment results were evaluated subjectively as well as objectively, Cetirizine and Astemizole were found to be more effective than Pheniramine maleate. The side effects were minimum with Cetirizine.

Since 1929, when Hansel emphasised the significance of allergic factor in many cases of rhinitis, various modes of treatment have been tried. In the absence of a definite cure, two general approaches are used; modification of environment to lessen or avoid antigen contact and the use of pharmacologic or

immunologic means to alter the response of nose to antigen. Avoidance of the offending antigen is the method of choice but this can seldom be achieved. Since many of the symptoms are considered due to local release of the inflammatory vasomediator-histamine, an antihistaminic is the preferred drug in the management of allergic rhinitis. The beneficial

effects of most antihistaminics are however offset by their associated adverse effects which may interfere with the daily routine of patient. Cetirizine and Astemizole both are new H₁ antagonists which are claimed to be devoid of anticholinergic or sedative actions (Callier et al., 1981 and Jubiin, 1988). Cetirizine also inhibits antigen antibody induced eosinophilic migration (Fedel et al., 1987). The present clinical trial was undertaken to compare the efficacy, safety and side effects of Cetirizine and Astemizole with those of Pheniramine maleate, a time tested antihistaminic in allergic rhinitis.

Material and Methods

A randomised study was conducted in Department of E.N.T., Institute of Medical Sciences, Banaras Hindu University, Varanasi in 60 established cases of allergic rhinitis. The patients were divided in three groups of twenty patients each. Only those cases were included

in the study which were not receiving any medication for any other disease. Prior to starting the treatment complete E.N.T. and general examination was done. All patients had routine blood and urine analysis alongwith skiagrams of the para nasal sinuses. In all the cases nasal smear was taken and tested for presence of eosinophils. The nasal smear in allergic rhinitis is generally loaded with eosinophils (Mygind, 1978). The absence of eosinophils in a particular smear does not rule out allergy, but their presence during an allergic episode is strong evidence to confirm it (Fagin et al., 1981). The number of eosinophils in nasal smear was recorded using the Ozala et al. (1982) criteria for quantification :

- Nil = No cell in any high power field
- + = 1 to 3 cells in some high power fields
- ++ = Some cells in most high power fields
- +++ = Many cells in all fields.

Table I
Effect of Treatment : Subjective Evaluation

Sl. No.	Complaints	Gpa n = 17			GpB n = 19			GpC n = 19		
		Total Relief	Improved	No Change	Total Relief	Improved	No Change	Total Relief	Improved	No Change
1.	Nasal Obstruction	7 (41.18%)	8 (47.05%)	2 (11.77%)	10 (52.63%)	7 (36.84%)	2 (10.53%)	12 (63.16%)	6 (31.58%)	1 (5.26%)
2.	Rhinorrhoea	7 (41.18%)	6 (35.29%)	4 (23.53%)	12 (63.16%)	6 (31.58%)	1 (5.26%)	15 (78.95%)	4 (21.05%)	-
3.	Sneezing	5 (29.41%)	9 (52.94%)	3 (17.65%)	10 (52.63%)	8 (42.11%)	1 (5.26%)	14 (73.68%)	5 (26.32%)	-

Table II

Effect of Treatment : Objective Evaluation Eosinophils in Nasal Smear

Sl. No.	Group	Eosinophil Count in Nasal Smear							
		Pre Treatment				Post Treatment			
		NIL	+	++	+++	NIL	+	++	+++
1.	Group A n = 17	3 (17.65%)	2 (11.77%)	6 (35.29%)	6 (35.20%)	4 (23.53%)	4 (23.53%)	6 (35.29%)	3 (17.65%)
2.	Group B n = 19	3 (15.79%)	3 (15.79%)	6 (31.58%)	7 (36.84%)	6 (31.58%)	6 (31.58%)	4 (21.05%)	3 (15.79%)
3.	Group C n = 19	4 (21.05%)	2 (10.53%)	7 (36.84%)	6 (31.58%)	7 (36.84%)	7 (36.84%)	3 (15.79%)	2 (10.53%)

All medications were discontinued one week prior to starting the treatment. In group A, 75 mg of Pheniramine maleate in sustained release form was administered at bed time. In group B, 10 mg of Astemizole was given one hour before dinner and in group C, 10 mg of Cetirizine was advised once a day. Decongestant nasal drops were strictly avoided. Patients were instructed to take steam inhalations in case of extreme nasal blockage. All these medications were advised for 15 days.

Patient Assessment : The patients were reviewed weekly. Their symptoms and clinical parameters as per study protocol were assessed on completion of treatment. A three point scoring scale (0 - absent, 1 - mild to moderate and 2 - severe) was used to assess the patients symptoms like nasal obstruction, rhinorrhea and sneezing. Apart from this nasal smear was also examined for eosinophils at each visit.

Patients were specially questioned for any side effects such as dryness of mouth, drowsiness, sedation, confusion, inability to concentrate, increased appetite or gastrointestinal disturbances etc. The side effects if reported were properly recorded.

Observations

Sixty patients, 37 males and 23 females between 17-51 years of age constituted the material for the study. Five patients, three from Pheniramine group and one each from Astemizole and Cetirizine group failed to complete the treatment and excluded from the study. The results were evaluated in 55 patients only. Out of these 17 patients were from group A and 19 patients

each were from group B and C. The results were analysed as shown in Table I and II. As per subjective evaluation in results were better in Cetirizine and Astemizole groups in comparison to Pheniramine group. While 61.16%, 78.95% and 73.68% patients in Cetirizine group claimed complete relief in nasal obstruction, rhinorrhoea and sneezing respectively, another 31.58%, 21.05% and 26.32% patients reported improved airway, decreased rhinorrhoea and decreased frequency of sneezing after completion of treatment.

In Astemizole group 56.63%, 63.16% and 52.63% patients observed complete relief and another 36.84%, 31.59% and 42.11% patients had improvement in their symptoms of nasal obstruction, rhinorrhoea and sneezing respectively. In contrast to these in Pheniramine group relief in symptoms of nasal obstruction, rhinorrhoea and sneezing was noticed by 41.18%, and 29.41% patients only. The onset of effect of drug was late in case of Astemizole group in comparison to Cetirizine group. While in Cetirizine group effect started within one day, in Astemizole group it appeared only of fourth or fifth day.

Decrease in eosinophil count in nasal smear was observed in all the groups, but it was more marked in Cetirizine and Astemizole groups, (Table II). In over all evaluation after completion of treatment 57.90% patients in cetirizine group, 42.11% in Astemizole group and 17.65% patients in Pheniramine reported excellent results and 5.26% in Cetirizine group, 10.53% in Astemizole group and 23.59% patients in Pheniramine group showed poor response to the treatment (Table III).

Table III

**Overall Evaluation on Completion of Treatment
(Subjective Evaluation)**

Sl. No.	Response	Group A n = 17	Group B n = 19	Group C n = 19
1.	Excellent	3 (17.65%)	8 42.11%	14 (57.40%)
2.	Good	10 (58.82%)	9 (47.36%)	7 (36.84%)
3.	Poor/No Response	4 (23.53%)	2 (10.53%)	1 (5.26%)

The side effects were also much less with Cetirizine and Astemizole groups (Table IV). Although sedation, dryness of mouth and tiredness were more commonly observed with Pheniramine group, some patients who received Astemizole, also complained these effects. In Cetirizine group only side effect which was reported by patients was sedation. One patient (5.26%) of Astemizole group also complained of increase in appetite and one patient (5.88%) in Pheniramine group complained of palpitation and nervousness. Gastrointestinal disturbances were not reported by any patient. Adverse effects on laboratory data were also not observed in any of the groups.

Discussion

Cetirizine and Astemizole are both newer H₁ receptor sites and their reliable and consistent inhibition of histamine induced allergic reactions (Richards, 1990).

In comparison to pheniramine maleate the side effects were also much less with Cetirizine and Astemizole (Table IV). However, in our study incidence of side effects were much higher in comparison of previous reported studies in whom Cetirizine and Astemizole were claimed to be devoid of CNS side effects and anti cholinergic effects (Callier et al., 1981), Wilson and Hillas (1982), Nicolson et al., 1982 and Vijay et al., 1994). The higher incidence of these side effects in our study might be because of the fact that we specifically asked regarding these effects from all such patients who failed to volunteer any adverse effects of the drug. Most of the patients acknowledged that they did not tell themselves regarding these effects because after experiencing so many antihistaminics for a long duration for their ailment, they now felt these side effects as a necessary evil.

Our study reveals that Cetirizine and Astemizole both

Table IV

Side Effects				
SL. No.	Side Effect	Group A n = 17	Group B n = 19	Group C n = 19
1.	Sedation	9 (52.94%)	2 (10.53%)	4 (21.05%)
2.	Dryness of Mouth	7 (41.18%)	2 (10.53%)	-
3.	Tiredness	6 (35.29%)	1 (5.26%)	-
4.	Others	1* (5.88%)	1** (5.26%)	-

* Palpitation and nervousness

** Increase in appetite

Present study shows that Cetirizine and Astemizole are definitely more effective than Pheniramine maleate in allergic rhinitis. While excellent results were reported in 57.90% patients with Cetirizine and in 42.11% with Astemizole, with Pheniramine maleate only 17.65% patients reported excellent results (Table III). However in Astemizole there was a lag period of almost five days for beneficial effects to appear. Other workers also reported this lag period (Laduron et al., 1982 and Bhanu et al., 1989). This might be because of long elimination half life of Astemizole (Howrath et al., 1984).

are more effective than pheniramine maleate in allergic rhinitis. The better effect of Cetirizine may be attributed to its dual action as it prevents chronic inflammation by inhibiting eosinophil chemotaxis. However more clinical trials with larger number of patients and longer follow ups must be performed before concluding about the Cetirizine Astemizole comparison.

Acknowledgement

To M/s Cadila Chemicals Ltd., Ahmedabad for providing the necessary drugs for the trial.

References

1. Bhanu, T.S., Thariyan, M. and Thomas, M. (1989) : Comparative Study of Astemizole - A New H₁ Antagonist with a Conventional Antihistaminic in Patients with Allergic Rhinitis. *Ind. J. Otolaryng.*, 41 : 108 -110.
2. Callier, J.; Engelen, R.F, Ianniello, I. (1981) : Astemizole in Hay Fever. An International Double Blind Study Comparing a weekly Treatment with a placebo. *Current Therapeutic Research*, 29 : 24 - 29.
3. Fagin, J. F ; Roger, F. and Fireman, P. (1981) : Allergic Rhinitis. *Paediatrics Clinics of North America*, 28 : 797 - 806.
4. Fedel, R.; Herpin, R.N.; Riboux, J.P. (1987) : Inhibitory Effect of Cetirizine 2 HCL on Eosinophil Migration in Vivo. *Clin. Allergy*, 17 : 373 - 379.
5. Hansel, F.K. (1929) : Histopathologic Studies of Nose and sinuses in Allergy. *J. Allergy*, 1 : 43.
6. Howrath, P.H.; Emmanuel, M. B. and Holgate, S. T. (1984) : Astemizole a Potent Histamine H₁ Receptor Antagonist Effect in Allergic Rhinoconjunctivitis on Antigen and Histamine Induced Skin Weal Responses and Relations to Serum Levels. *Brit. J. Clin. Pharmacol.*, 18 : 1 - 9. (1988)
7. Jublin, J: A Treatment of Chronic Urticaria with Cetirizine dihydrochloride, Non sedative Antihistaminic. *Br. J. Dermatol.*, 119 : 67 - 71.
8. Laduron, P. M. : Janssen, P.F.M.; Gommeren, W. and Laysen, J. E. (1982) : In vitro and in vivo Binding Characteristics of a New Long Acting Histamine H₁ Antagonist, Astemizole. *Mole Pharmacol.*, 21 : 294 - 300.
9. Mygind, N. (1978) : Nasal Allergy. Blackwell scientific publication.
10. Nicolson, A.N.; Smith, P.A. and Spencer, M.B. (1982) : Antihistamines and Visual Function Studies on Dynamic Activity and the papillary Response to Light. *Brit. J. Clin. Pharmacol.*, 14 : 683 -690.
11. Ozala, K.; Sipila, P.; Sorri, M. and Karma, P. (1982) : Role of Allergy in Chronic Otitis Media. *Acta Otolaryngologica.*, 93 : 55.
12. Richards, D.M. et al (1990) : *Drugs*. 40 (5) : 762 - 781.
13. Vijay, M.; Rawal, R.C. and Billimona, P.E. (1994) : A Comparative Study of Efficacy of Cetirizine versus Astemizole in Chronic Idiopathic Urticaria. *Ind. J. Dermatol. Venereol. Leprol.*, 60 : 272 - 274.
14. Wilson, J. D. and Hillas, J.L. (1982) : Astemizole a New Long Acting Antihistamine in the Treatment of Seasonal Allergic Rhinitis. *Clinical Allergy*, 12 : 131 -140.