Double-Blind Comparison of the Efficacy and Safety of Astemizole and Loratadine in the Treatment of Seasonal Allergic Rhinitis

The LASAR (Loratadine and Astemizole in Seasonal Allergic Rhinitis) Study Group†

Summary

469 adult patients were randomised to 1 of 2 parallel double-blind treatment groups to evaluate the comparative efficacy and safety of astemizole 10mg and loratadine 10mg once daily for 3 weeks in seasonal allergic rhinitis. Rescue medication was prohibited.

Strong and consistent within-treatment effects were identified for both drugs in the 446 patients evaluable for efficacy. Response to astemizole treatment was 88% and significantly greater than with loratadine (80%). Overall symptom relief was rated as significantly superior by both the investigator and patient for astemizole versus loratadine. Symptom scores were particularly responsive to astemizole treatment with statistically significant separation from loratadine identified for the majority of efficacy parameters at most time-points. Adverse experience reports were comparable in the 2 treatment groups. Both treatments were associated with a statistically significant bodyweight gain (0.25kg).

Both astemizole and loratadine were effective and well tolerated in the symptomatic management of seasonal rhinitis; astemizole demonstrated a consistently greater degree of efficacy compared with loratadine.

Astemizole and loratadine belong to the ‘second generation’ group of H1-receptor antagonists characterised by a relatively low propensity to cause anticholinergic side effects, sedation and other adverse effects on the central nervous system (Druce 1990). As a class, these new antihistamines are gradually replacing traditional H1-antagonists as first-line therapy in the management of common allergy disorders (Simons 1990). There have been only a few clinical therapeutic trials in which the second generation antihistamines have been directly compared, primarily because of the large sample size that is required to detect subtle, yet potentially clinically important, differences in efficacy among members of this class of compounds.

Both astemizole and loratadine are potent and specific antagonists at peripheral H1-receptor sites (Ahn & Barnett 1986; Laduron et al. 1982). There are, however, considerable differences in their pharmacokinetic and pharmacodynamic properties (Mann et al. 1989). These inherent differences in the compounds, coupled with such variables as dose and dose regimen, have made the data obtained from clinical pharmacological models such as the histamine challenge skin test difficult to interpret and extrapolate, and have also made it difficult to predict their effects in clinical practice.

† A list of participants and their centres is given at the end of the article.
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(Gendreau-Reid et al. 1986; Kassem et al. 1988; Simons et al. 1990). Despite this limitation, several generalisations and hypotheses have been put forth based on pharmacokinetic/pharmacodynamic studies regarding such features as onset and duration of action, potency, and adverse effect profile of astemizole and loratadine in the clinical setting (Gendreau-Reid et al. 1986; Kassem et al. 1988; Rihoux et al. 1990; Simons et al. 1990).

Both astemizole and loratadine have been shown to be effective versus placebo and reference H1-antagonists in the management of the 3 core allergic indications: seasonal allergic rhinitis, perennial allergic rhinitis and chronic idiopathic urticaria (Bernstein & Bernstein 1986; Brobyn et al. 1982; Bruttmann et al. 1987; Dockhorn et al. 1987; Knight 1985; Paul 1988). However, no large scale clinical trial has been conducted to definitively compare the relative efficacy and safety of these agents at recommended therapeutic dosages. The objective of this study was to clearly define the comparative antihistamine efficacy and safety of astemizole 10mg once daily and loratadine 10mg once daily in adult patients with symptomatic seasonal allergic rhinitis.

 Patients and Methods

Subjects

14 centres throughout Mexico participated in this double-blind comparative study from August 1988 to January 1990. Male and female outpatients aged more than 12 years with a 2-year history of seasonal allergic rhinitis and who presented with a minimum total qualifying symptom (rhinorrhoea, sneezing, itchy eyes) score at baseline (post-washout) were considered eligible for entry into the trial. Patients with moderate to severe asthma, vaso- motor rhinitis, recent (less than 3 months) variation in hyposensitisation therapy, inability to comprehend the protocol or communicate with the investigator, or plans to travel outside the pollen area for 3 or more days of 1 or more study weeks were excluded. Pregnant, nursing and fertile women not using adequate contraception were also excluded. All patients gave witnessed verbal informed consent prior to enrolment.

Treatment Plan

Patients were required to discontinue previous antiallergic medication(s) and complete an appropriate washout period prior to the baseline visit and randomisation: antihistamines (except astemizole) and decongestants – 3 or more days; astemizole – 6 or more weeks; oral or topical corticosteroids and sodium cromoglycate – 14 or more days; and injectable steroids – 30 or more days. Eligible patients were randomised to 1 of 2 parallel double-blind treatment groups to receive either astemizole 10mg or loratadine 10mg once daily for 21 days. All study medication was encapsulated to maintain double-blinding. Patients were instructed to take the study drug in the morning. There were 4 scheduled visits: baseline/randomisation (day 0), and weekly on treatment follow-up visits (week 1, week 2, week 3). Any medication intended for the relief of allergy symptoms (rescue medication) was prohibited throughout the entire study period.

Assessments

The severity of 7 rhinoconjunctivitis symptoms (rhinorrhoea, sneezing, itchy nose, congestion, itchy/gritty eyes, lacrimation, eye redness) was evaluated by investigators at each visit on a 4-point categorical rating scale (0 = none, to 3 = severe). The total symptom score (7 symptoms) could range from 0 to 21. At randomisation (post-washout), patients were required to have a minimum total score for the 3 qualifying symptoms of at least 5. Patients recorded the severity of each qualifying symptom daily in a diary on a 100mm visual analogue scale (VAS) ranging from 'no symptoms' to 'severe symptoms'. Investigators and patients rated the severity of combined ocular and nasal symptoms at each visit on a similar VAS. At termination, patient disposition was categorised and a global evaluation of the efficacy of the study drug was performed by the investigator and patient on