Poster 601

Oral vapitadine, a new non-sedating antihistamine, relieves itch associated with atopic dermatitis

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Introduction

Itch is an essential feature of atopic dermatitis and one of its most troublesome symptoms. Despite the frequent use of oral H_1antihistamines, their role in the treatment of itch in atopic dermatitis remains controversial and the beneficial effects are often attributed to their sedative properties.

Vapitadine (R129160; Hivenyl™) is a new selective, non-sedative H_1 antihistamine. In several *in vitro* and *in vivo* pharmacological models, vapitadine is at least as potent as cetirizine (Zyrtec®) and does not penetrate the blood-brain barrier (Janssens *et al*, 2005).

In healthy volunteers vapitadine dose-dependently inhibits the histamine-induced wheal and flare reaction (Beetens *et al*, 2007). The compound shows a fast onset of action (within 1 hour) as well as a long-lasting (>24 hours) antihistaminic activity (from 10 mg onwards). Vapitadine does not induce sedation up to the highest dose tested (150 mg o.d. for 8 days).

As such, vapitadine is a suitable tool to explore the activity of H_1 antihistamines in different dermatological indications, without the sedative effect often observed with other antihistamines when increasing the doses.

Objectives

To assess the efficacy of oral vapitadine on the alleviation of itch in patients with atopic dermatitis using concomitantly a weak topical corticosteroid. To assess the safety and tolerability of oral vapitadine in atopic dermatitis patients.

Patients and methods

Design: randomized, placebo-controlled, double-blind, multi-centre exploratory trial. After a one-week run-in period, 43 adult patients with atopic dermatitis were randomized to treatment with oral vapitadine 60 mg twice daily (n=22) or placebo (n=21) for one week. Final evaluations were done at the end of treatment. All patients applied daily 1% hydrocortisone acetate cream and an emollient throughout the run-in and treatment period.

Evaluations/Assessments: during run-in as well as during treatment period, patients evaluated twice daily (using a diary) their itch symptoms (Visual Analog Scale; 100 mm horizontal line, labeled "no itch" at left end, 0 mm, and "worst imaginable itch" at right end, 100 mm) and sleep pattern in the morning (4-point scale ranging from 0 (no effect on sleep) to 3 (severe effect on sleep)). Physicians evaluated the itch on a 7-point scale, ranging from 0 ("no itch") to 6 ("severe itch") and the extent and severity of the atopic lesions using the EASI score (baseline and end of treatment). At the end of the trial, patients as well as physicians evaluated itch relief on a 9-point scale ranging from -4 ("extreme deterioration") to +4 ("almost complete to complete relief").

Approval: was obtained from an Independent Review Board and written informed consent was obtained from all patients.

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Efficacy Results

Evaluation of itch and itch relief

Patients evaluated their itch symptoms twice daily using a diary (itch VAS score) and at the end of the treatment as the itch relief score. Vapitadine significantly (p=0.041) reduced the daily VAS itch score in comparison to placebo (table 1). Furthermore, itch relief was significantly (p=0.008) more pronounced in the vapitadine group than in the placebo group (table 1). Interestingly, nine of 22 patients reported either a marked improvement (+3) or almost complete to complete relief (+4) of their itch symptoms versus none in the placebo group (figure 1).

Table 1: Evaluation of itch symptoms by patients

	Placebo N=21	Vapitadine N=22	P-value *
Itch VAS score (mean changes from baseline)	-4.9	-14.8	0.041
Itch relief score (mean)	0.2	1.6	0.008

** Two-sided P-value of Wilcoxon-Mann-Whitney test comparison with placebo*

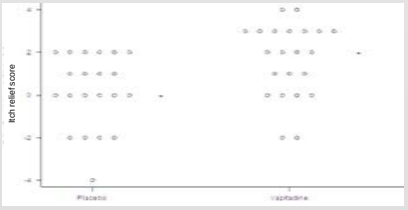

Figure 1: Frequency distribution of subject's itch relief scores

At the end of the treatment period the subject evaluated the change in itch symptoms in comparison to baseline level and gave a score (-4 to 4) for itch relief; the higher the score, the greater the relief. Each point represents the score for an individual subject.

Physician's assessments of itch and itch relief showed a tendency in favor of vapitadine, however statistical significance was not reached (Table 2).

Table 2: Evaluation of itch symptoms by physicians

	Placebo N=21	Vapitadine N=22	P-value *
Itch score (mean changes from baseline)	-0.6	-1.2	0.343
Itch relief score (mean)	0.3	1.3	0.067

** Two-sided P-value of Wilcoxon-Mann-Whitney test comparison with placebo*

Evaluation of atopic lesions

Signs and symptoms of the atopic lesions improved as well in the placebo group (-6.1 EASI points) as in the vapitadine group (-4.7 EASI points). The difference between both treatment groups is not statistically significant (p=1.0).

Evaluation of sleep pattern

Every morning the patient reported the effect of the itch on the sleep quality in the diary. During the treatment week the sleep quality slightly improved in both groups. Although the improvement was more pronounced in the vapitadine group (-0.36) than in the placebo group (-0.12), the difference was not statistically significant (p=0.311).

Safety Results

Adverse Event (AE): no serious AE occurred during the trial. Overall, the incidence of AEs was low: four (gastroenteritis, cough, eosinophilia, exacerbation of atopic dermatitis) in the placebo group and two (eye infection, pharyngitis) in the vapitadine group. AEs in the vapitadine group were considered mild and not related to trial medication.

Neither sedation nor somnolence was reported.

ECG evaluation: no clinically important post-treatment changes in ECG morphology or relevant differences in mean change of ECG intervals versus screening in the two groups were observed.

Clinical laboratory safety: no clinically relevant trends in clinical laboratory test results from screening to end of treatment were observed.

Conclusion

In this one-week placebo-controlled trial vapitadine, on top of treatment with hydrocortisone acetate cream and emollient, significantly improved the itch symptoms in atopic dermatitis patients. No significant effect of vapitadine on the improvement of the extent and severity of the atopic lesions and the sleeping pattern was observed. The treatment was well tolerated and no sedation was reported.

These exploratory trial results warrant further studies with an enlarged trial population and a prolonged treatment period to determine the effect of vapitadine on the other signs and symptoms of atopic dermatitis .

Reference

Beetens J *et al*, Ann Allerg Asthma Immunol, 98 (S1), 2007

Janssens F *et al*, J Med Chem., 48, 2154, 2005

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