

1.1. Desloratadine and increased appetite

Introduction

Desloratadine is a non-sedating, long-acting histamine antagonist with selective peripheral H1-receptor antagonist activity. It is the primary active metabolite of loratadine. The antihistaminergic activity of desloratadine is 2.5 - 4 times greater than loratadine [1]. After oral administration, desloratadine selectively blocks peripheral histamine H1- receptors because the substance is excluded from entry to the central nervous system [2].

Desloratadine has been approved for the Dutch market since January 2001. It is indicated for *the relief of symptoms associated with allergic rhinitis and urticaria*. The most frequent adverse events reported in excess of placebo were fatigue (1.2 %), dry mouth (0.8 %) and headache (0.6 %). In a clinical trial with 578 adolescent patients, 12 through 17 years of age, the most common adverse event was headache; this occurred in 5.9 % of patients treated with desloratadine and 6.9 % of patients receiving placebo [2].

The current observation describes the association between desloratadine and increased appetite. Increased appetite is mentioned with an incidence of 0.5 % in the Summary of Product Characteristics (SmPC) of loratadine (Claritin®) [3].

Desloratadine is available in the Netherlands and the EU as Aerius® and elsewhere in the EU possibly also as Azomyr® and Neoclarityn®, in the following pharmaceutical forms: film-coated tablets 5 mg, orodispersible tablets 2.5 and 5 mg and oral solution 0.5 mg/ml [2,4,5].

Reports

On March 21, 2011 the database of the Netherlands Pharmacovigilance Centre Lareb contained 2 reports concerning increased appetite and one with increased carbohydrate craving associated with the use of desloratadine. The reports are listed in Table 1. All cases were reported by general practitioners. Two cases involved women, in the third case a young girl was involved. In all patients desloratadine was used to treat allergic symptoms. The latency in all patients was one or a few days. In patient A the increased appetite resulted in a weight increase of 2 kg in six weeks time. All patients recovered after discontinuation of desloratadine; in patient B a positive rechallenge was found.

Table 1. Reports of increased appetite associated with the use of desloratadine

Patient, Sex, Age	Drug Indication for use	Concomitant medication	Suspected adverse drug reaction	Time to onset, Action with drug outcome
A 53784 F, 41-50 years	desloratadine tablet 5mg allergy NOS	not reported	appetite increased nos weight increase	days discontinued recovered
B 64726 F, 41-50 years	desloratadine tablet 5mg allergy	not reported	carbohydrate craving	1 day discontinued recovered
C 112075 F, 8-10 years	desloratadine tablet 5mg allergy	not reported	appetite increased nos	days discontinued recovered

Other sources of information

SmPC

Increased appetite is not mentioned in either of the SmPCs of the Dutch desloratadine containing products (Aerius[®], Azomyr[®] and Neoclarityn[®]) [2,4,5], although this is described in the SmPCs for loratadine (Claritin[®]) [3].

Literature

Appetite stimulation is known for cetirizine, astemizole, azelastine (2nd generation antihistamines). Cetirizine produces a significant increase in postprandial glucose and a small rise in fasting glucose. Clemastine produced a small fall in fasting glucose and a small rise in postprandial blood glucose. The mechanism of these effects is not known. No information for desloratadine in association with increased appetite was found. In contrast, for loratadine increased appetite is described on several Dutch drug information websites; the Farmacotherapeutisch Kompas and the Informatorium Medicamentorum [1,6] and in the US SmPC [7].

Databases

On March 21, 2011, the database of the Netherlands Pharmacovigilance Centre only contained two reports of increased appetite in association with desloratadine; due to this low number of reports no reliable Reporting Odds Ratio (ROR) could be calculated. Also for the one report of carbohydrate craving no ROR was calculated.

The WHO database of the Uppsala Monitoring Centre contained 8 reports of increased appetite in association with desloratadine with a ROR of 2.7 (95 % CI 1.3- 5.3), which was disproportional. Four of these patients had a positive dechallenge, for one a positive rechallenge was observed.

On April 20, 2011, the Eudravigilance database contained 4 reports of increased appetite associated with the use of desloratadine, which was reported disproportionally (ROR = 5.8, 95% CI: 2.2 – 15.6). It concerns three females and one male. The median age of the patients was 23 years (range 10 - 49). Two reports were considered to be serious.

Prescription data

The number of patients using desloratadine in the Netherlands is shown in table 2 [8]

Table 2. Number of patients using desloratadine in the Netherlands between 2005 and 2009

Drug	2005	2006	2007	2008	2009
desloratadine	324,300	416,280	452,450	461,280	509,270

Mechanism

It has been suggested that modified histamine and/or H1 receptor concentrations are potential mechanisms for elevated central histaminergic activity in food intake-related pathophysiological states [9]. Especially antihistamines with a strong antiserotonergic effect will raise the appetite [6,10]. Second generation antihistamines are relatively free from anticholinergic, antiserotonergic and alpha-

adrenergic activity; for desloratadine however, some anticholinergic effect has been described [11].

Desloratadine is the active metabolite of loratadine. Similar to loratadine, desloratadine is a nonsedating antihistamine, although its elimination half-life is longer. In vitro, desloratadine has strong affinity for H1 receptors and 15 to 50 times less affinity for H2 and muscarinic receptors. In vitro, it down-regulates histamine, tryptase, cysteinyl leukotriene, and prostaglandin release from mast cells and basophils [12]. It is generally known that the histaminergic neuron system modulates appetite control beside wakefulness, the sleep-wake cycle, learning, memory and emotion [13].

Discussion and Conclusion

Lareb received two reports of increased appetite and one report of carbohydrate craving with the use of desloratadine within a few days after start. In all cases a positive dechallenge had been reported and in one case also a positive rechallenge was observed. For other second generation antihistamines an increase in appetite was reported fifteen times, of which three times with loratadine use. The association of increased appetite with the use of desloratadine was supported by a statistically significant disproportionality in the WHO and Eudravigliance databases. It is known that antiserotonergic antihistamines stimulate appetite and some 2nd generation antihistamines have been observed for such an effect. Although no supportive literature had been found for this association with the active metabolite desloratadine, for loratadine itself, the association is mentioned in the US and Dutch SmPC, as well as on Dutch drug information websites.

- Possible new signal of increased appetite in association with the use of desloratadine. Due to similarity of desloratadine with loratadine, it should be considered to mention increased appetite in the SmPC of desloratadine as well.

References

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This signal has been raised on July 2011. It is possible that in the meantime other information became available. For the latest information please refer to the website of the MEB www.cbgmeb.nl/cbg/en/default.htm or the responsible marketing authorization holder(s).