Use of first-generation antihistamines in the treatment of NAR

Patients with NAR and AR experience similar symptoms including nasal congestion, postnasal drainage and rhinorrhea although through different mechanistic pathways.[296] Responses to various treatments in NAR and AR may vary.[297] A major symptom of patients with NAR that is frequently not well controlled despite combination topical nose sprays with anticholinergic activity is postnasal drainage.[296] There are no DBPC trials evaluating the therapeutic efficacy and safety of first-generation oral antihistamines such as chlorpheniramine maleate for the treatment of NAR/VMR. In a risk/benefit assessment, mindful of (1) the considerable concerns about safety of first-generation antihistamines as reviewed under discussion for Recommendation 6, and (2) recognition that it is not possible in a standard office setting to accurately assess development of some clinical adverse effects from these agents (eg, development of subtle changes in cognition or other potential central nervous system side effects such as decreased reaction time), some clinicians suggest that monitored use of first-generation oral antihistamines as an adjunctive anticholinergic agent may be considered in patients with NAR who have bothersome postnasal drainage refractory to other therapies. The decision to use first-generation antihistamines for NAR remains controversial, should be individualized, and should involve a physician and patient–shared decision-making discussion, reviewing the potential risks and benefits, and patient preferences. If first-generation oral antihistamines are used to treat postnasal drip in VMR/NAR, patients should be carefully monitored for any clinically observable side effects, the lowest effective dose should be used, and these agents should be discontinued when side effects are identified. Special consideration/caution should be taken into account using these agents in frail elderly patients,[298] individuals with existing known chronic disorders (dementia, Alzheimer's, benign prostatic hyperplasia) that would be complicated by their use or those working in occupations involving heavy machinery, driving, or flying.

Oral leukotriene receptor antagonists

Recommendation 7. *CBS:* We suggest that the clinician not select the oral leukotriene receptor antagonist (LTRA) montelukast for the initial treatment of AR due to reduced efficacy when compared with that of other agents. Furthermore, serious neuropsychiatric events that may include suicidal thoughts or actions have been reported in some patients taking montelukast. As advised by the FDA, montelukast should be used to treat AR only in patients who are not treated effectively with or cannot tolerate other alternative therapies.

Strength of recommendation: Conditional

Certainty of evidence: Very low

Recommendation 8. *CBS:* We recommend that the clinician not select an oral LTRA for the treatment of NAR.

Strength of recommendation: Conditional

Certainty of evidence: Ungraded as there are no studies.

Note: Unanimous vote in favor by work group and JTFPP.

LTRAs are modestly effective in the treatment of SAR and PAR.[299-302] Multiple systematic reviews have concluded that LTRAs have effectiveness similar to oral antihistamines with loratadine as the usual comparator,[301,303-306] but others find that LTRAs are less effective than antihistamines.[306] LTRAs are less effective than INCS.[301,304-306] Considering that the LTRA montelukast is equally or less effective than oral antihistamines for AR and is less effective than INCS (which would be preferred therapy for more severe AR because of greater effectiveness), clinicians should not routinely offer an LTRA as preferred therapy for patients with AR. Furthermore, as discussed below, serious neuropsychiatric events that may include suicidal thoughts or actions have been reported in some patients taking montelukast. As advised by the FDA, montelukast should be used to treat AR only in patients who are not treated effectively with or cannot tolerate other alternative therapies.[307] In such patients, when considering montelukast, a shared-decision making conversation should be utilized.

The use of an oral LTRA in combination with an oral antihistamine may be more effective than monotherapy with an LTRA (montelukast) for AR, although not all study results are consistent with this finding.[304,308,309] The combination of an oral LTRA and an oral antihistamine is similarly effective as monotherapy with an INCS for AR though it is likely more costly and burdensome to maintain.[310,311]

There is no evidence to support the use of LTRAs in NAR. There is no mechanistic rationale or expert opinion that supports the use of an LTRA in NAR.

Montelukast has been approved down to 6 months of age. It is not associated with somnolence and side effects are uncommon.[312,313] However, there are postmarketing reports of rare drug-induced neuropsychiatric events including sleep disturbances, depression, anxiety, aggression, psychotic reactions, and suicidal thinking and behavior. Infants are more prone to drug-associated sleep disturbances; children present most often with symptoms of depression and anxiety; and adolescents are more prone to symptoms of depression, anxiety, and suicidal behavior.[314-317] Unexpectedly, a worldwide review of Individual Case Safety Reports associated with montelukast determined that completed suicides were reported more frequently for children than for adolescents or the total population.[316] Most studies are low-quality evidence, (eg, case reports or observational studies), mainly in children and adolescents; high-quality epidemiological studies are needed to evaluate the association and quantify the risk of neuropsychiatric adverse events, not only in children and adolescents, but also in adults.[317] It is advised that clinicians monitor patients who may be at elevated risk for suicidal ideation or psychiatric symptoms.

In patients with AR comorbid with asthma, compared with placebo, montelukast could result in significant improvements in both conditions and therefore can be considered an option for patients with both conditions.[310,318] However, due to the only modest efficacy and also the potential increased risks of montelukast compared with those of oral antihistamines, for the management of AR and comorbid asthma, the clinician should weigh the benefits of montelukast monotherapy versus an inhaled corticosteroid for asthma and an antihistamine or INCS for AR.

Systemic corticosteroids

Recommendation 9. *CBS:* We suggest that for the treatment of very severe or intractable AR, the clinician may consider a short course (5-7 days) of oral corticosteroids.

Strength of recommendation: Conditional

Certainty of evidence: Very low

Recommendation 10. *CBS:* We suggest that for the treatment of very severe or intractable AR, the clinician not prescribe a