for rhinitis, describe disease-associated problems more accurately and seem to be reflective of changes associated with therapeutic interventions.[258,261] VASs may also correlate well with rhinitis symptom scores and QOL measures, leading to improved symptom control.[254] There is also a highly significant correlation between a VAS and the Rhinoconjunctivitis Quality of Life Questionnaire. A subsequent study further validated the VAS and determined that changes in the VAS of 23 mm were found to be clinically significant.[254] A large European study found a smart phone app using the MASK (Mobile Airways Sentinel network)-Rhinitis VAS to be a reliable indicator of AR control and this control correlated well to work productivity.[262,263]

Control of AR

In addition to assessing AR severity and the impact on QOL, assessing control is an important goal. As has been shown to be helpful with asthma, AR severity can be measured in patients before treatment while measures of disease control are more applicable to optimize therapy in treated patients.[264] The Rhinitis Control Assessment Test, is a simple, reliable, self-administered 6-item questionnaire utilizing a 5-point Likert scale (Fig 1).[265-268] Developed to assist physicians in the assessment of patient rhinitis control in clinical practice, it also helps patients appreciate what rhinitis control is. The Rhinitis Control Assessment Test was developed and validated against total nasal symptom scores and the physician's global assessment. Subsequent work identified a cutoff score of 21 as representing good control, with a minimal important difference of 3. Downloadable forms for administering the Rhinitis Control Assessment Test are readily available online (eg, at AllergyAsthmaNetwork.org).

The Allergic Rhinitis Control Test is a validated 5-item self-assessment using a 5-point frequency scale with similarities to the Asthma Control Test.[103,269,270] The Control of Allergic Rhinitis and Asthma Test[25] is a validated 10-item questionnaire that was tested in patients consulting an allergist.[271-273] Limitations exist for control-based classifications as it is not clear whether AR control varies as a function of the disease-inducing allergen, and these questionnaires have not been validated in children.[32,264]

PHARMACOTHERAPY

Review of monotherapy and then combination pharmacologic therapeutic options for rhinitis (with an emphasis on treatment of AR) is presented first. Thereafter a stepwise pharmacologic treatment of AR will be presented, using algorithms for intermittent (Fig 2) and persistent (Fig 3) AR. Similarly, pharmacologic treatment algorithms have been developed for the management of intermittent (Fig 4) and persistent (Fig 5) NAR.

Review of pharmacotherapy classes for rhinitis

Oral antihistamines. Recommendation 6. *CBS:* We recommend against prescribing a first-generation antihistamine and are in favor of a second-generation antihistamine when prescribing an oral antihistamine for the treatment of AR.

Strength of recommendation: Strong

Certainty of evidence: High

Oral antihistamines are of established benefit in AR. The overall efficacy of first-generation antihistamines (eg, diphenhydramine, hydroxyzine, chlorpheniramine) compared with less sedating or nonsedating second-generation antihistamines (eg, cetirizine and levocetirizine, fexofenadine, loratadine and desloratadine) for the management of AR symptoms has not been adequately studied. However, selecting a second-generation antihistamine reduces the potential side effects including sedation, performance impairment, poor sleep quality, and anticholinergic-mediated symptoms (eg, dry eyes, dry mouth, constipation, urinary hesitancy, and retention) that have been associated with the first-generation antihistamines.[1]

First-generation antihistamines may produce performance impairment in school[274-276] and while driving[277-281] that can exist without subjective awareness of sedation,[282] and the use of first-generation antihistamines has been associated with increased automobile and occupational accidents.[277-281,283] Individual variation exists with respect to development of sedative effects with first-generation antihistamines.[276,284,285] One systematic review of first-generation antihistamines concluded that they induced nonamnestic deficits in attention and information processing.[286] One early study compared chlorpheniramine with placebo and found that drowsiness and dry mouth were greater with chlorpheniramine for the first 2 weeks, but after this time point, doses of chlorpheniramine <24 mg/day, compared with placebo, resulted in no significant difference in subjective drowsiness, dizziness, irritability, or dry mouth over the remaining 6 weeks of the study.[287] Other studies using chlorpheniramine as a comparator have reported similar increased symptoms of drowsiness, dry mouth, and dizziness for the first few days but tolerance to these subjective side effects of this medication occurred over time.[288-290] Tolerance to adverse central nervous system effects in an individual may or may not occur with regular daily use.[291] Although bedtime dosing of first-generation oral antihistamines has been suggested as a strategy to avoid daytime sedation, there can be residual central nervous system effects the next day because some agents have a very long terminal elimination half-life (>24 hours for chlorpheniramine).[292] Bedtime administration of first-generation antihistamines undesirably increased the latency to onset of restful rapid eye movement sleep and reduces the duration of rapid eye movement sleep.[291,293]

Beyond concerns about subjectively perceived side effects, among the anticholinergic side effects more recently reported in association with first-generation antihistamines is an associated higher risk of dementia. A 2015 US prospective population-based cohort study suggested a link between higher cumulative use of strong anticholinergics and the risk of developing dementia, with over 70% being diagnosed with Alzheimer's disease.[294] For dementia, adjusted hazard ratios for 10 years of cumulative anticholinergic use (including first-generation antihistamines, tricyclic antidepressants, and bladder antimuscarinics) compared with nonuse were 0.92 (95% CI, 0.74-1.16) for total standardized daily doses for 1 to 90 days, with a proportional increased risk for longer daily use, with a cumulative 3 years of daily use being 1.54 (95% CI, 1.21-1.96).[294] A longitudinal study showed that the use of anticholinergics in the elderly was associated with both reduced immediate recall and reduced executive functioning, which was associated in conjunction with increased brain atrophy manifest as reduced total cortical volume and temporal lobe cortical thickness and greater lateral ventricle and inferior lateral ventricle volumes.[295] These findings further support use of second-generation antihistamines over first-generation antihistamines for AR.