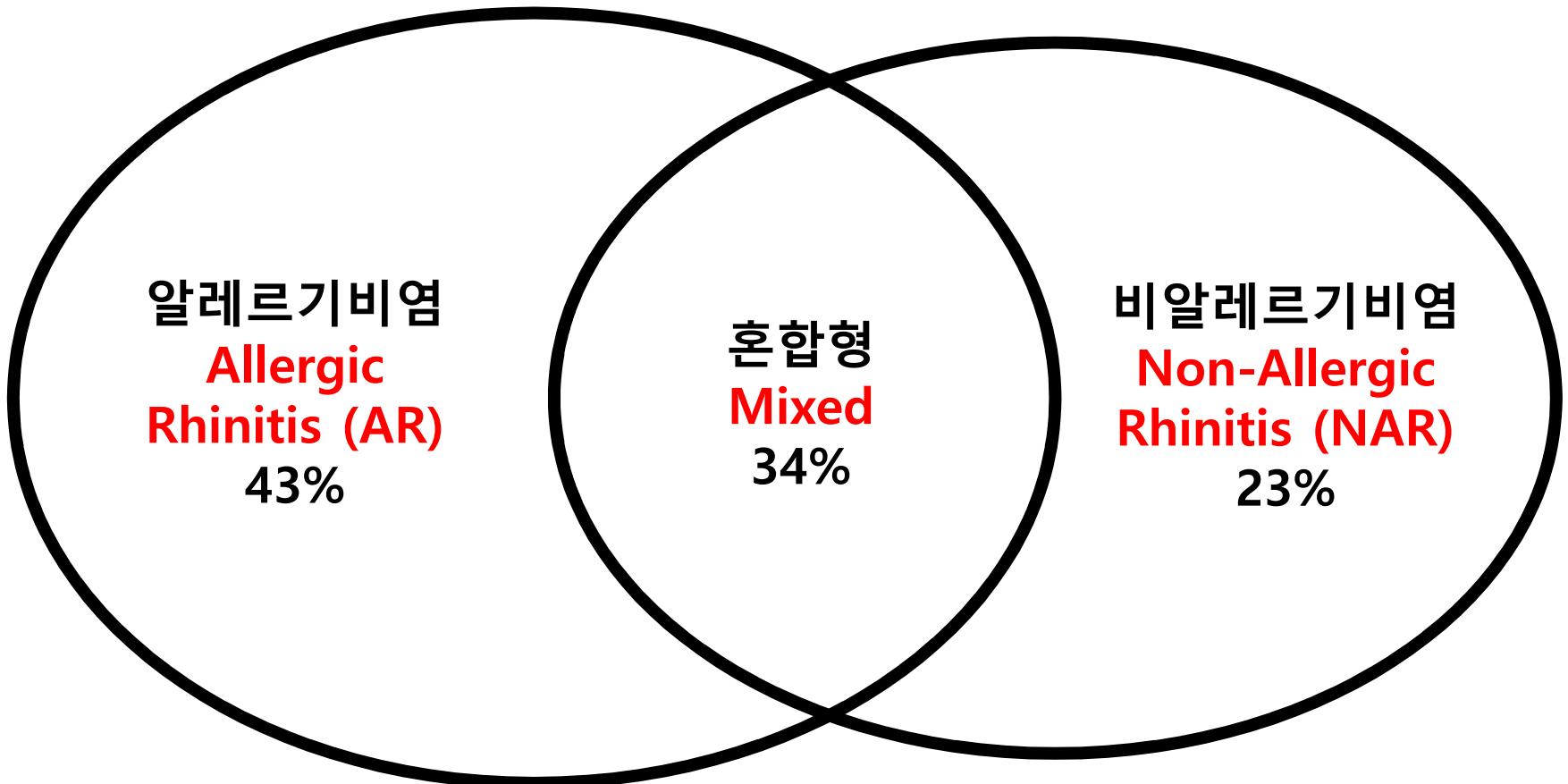


알레르기비염과 비알레르기비염: 약물요법 차이

전남의대 전남대병원 알레르기내과

고영일

비염: 분류



비염: 진단 알고리즘

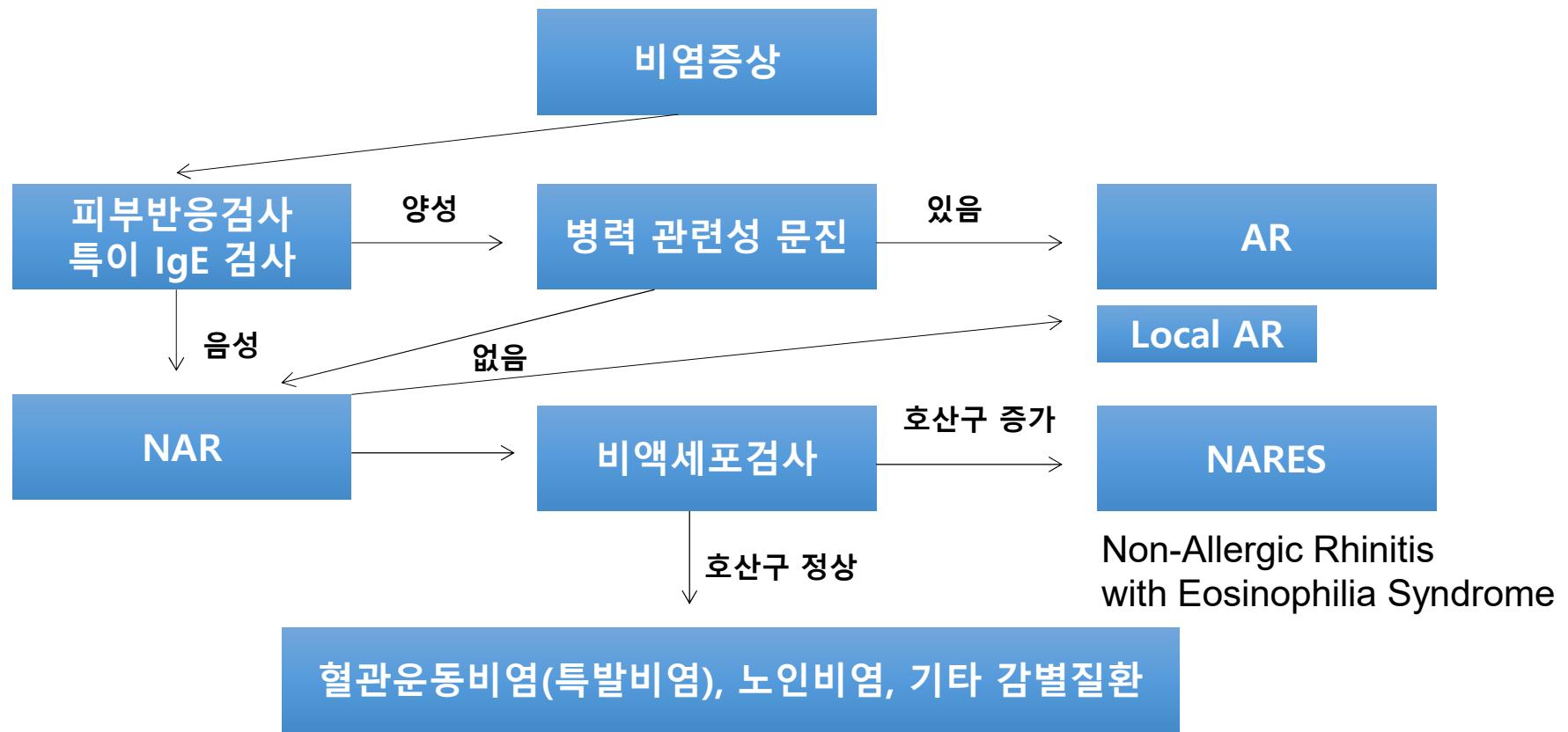
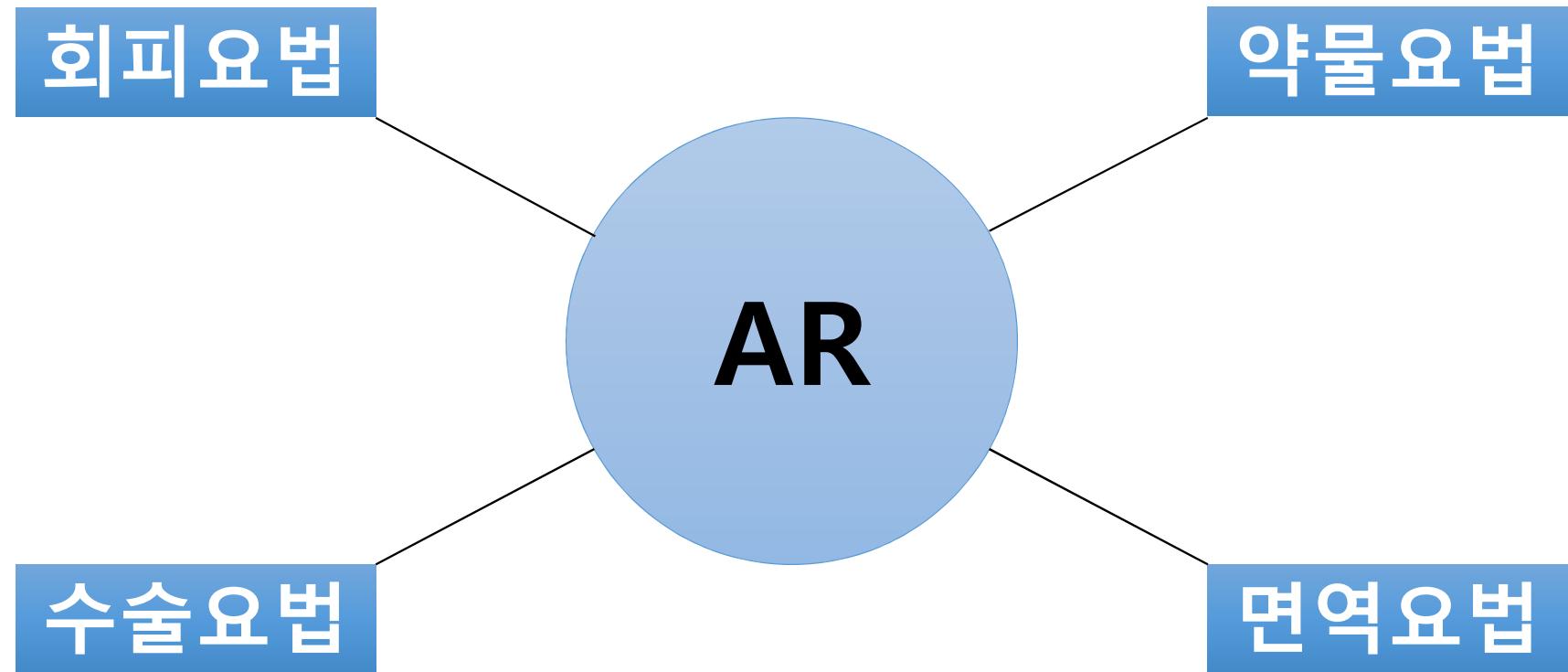


Table 3. Factors that significantly distinguish subjects with AR from subjects with NAR by backward stepwise logistic regression

Variable	OR	95% CI	p
Age	0.97	0.96–0.98	<0.0001
Presence of sneezing	4.09	2.78–6.00	<0.0001
Presence of nasal pruritus	3.84	2.60–5.67	<0.0001
Nasal symptoms			
Mild	0.21	0.09–0.49	0.0003
Intermittent/severe	3.66	2.06–6.50	<0.0001
VAS	1.05	1.03–1.07	<0.0001
Conjunctivitis	4.49	2.86–7.05	<0.0001
Effective response to antihistamines	22.59	13.79–37.00	<0.0001
PNIF	1.01	1.00–1.01	<0.0001
Nasal eosinophil counts	1.14	1.10–1.18	<0.0001

AR 치료



AR 약물들...

- 경구 항히스타민제: 2세대
- 비강내 항히스타민제(**INAH**)
- 비강내 스테로이드(**INS**):
가장 효과적
- LTRA: 천식과 동반
- 항콜린제(비강내): 콧물
- 충혈제거제(비강내, 경구):
코막힘

INAH: IntraNasal AntiHistamine

INS: IntraNasal Steroid

LTRA: LeukoTriene Receptor Antagonist

AR 중증도 분류

Intermittent

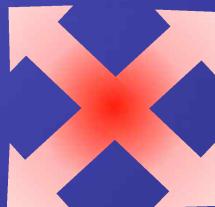
- < 4 days/week
- or < 4 weeks

Persistent

- \geq 4 days/week
- and \geq 4 weeks

Mild

- No impairment of daily activities, sports, leisure
- Normal school and work
- No troublesome symptoms



Moderate/Severe

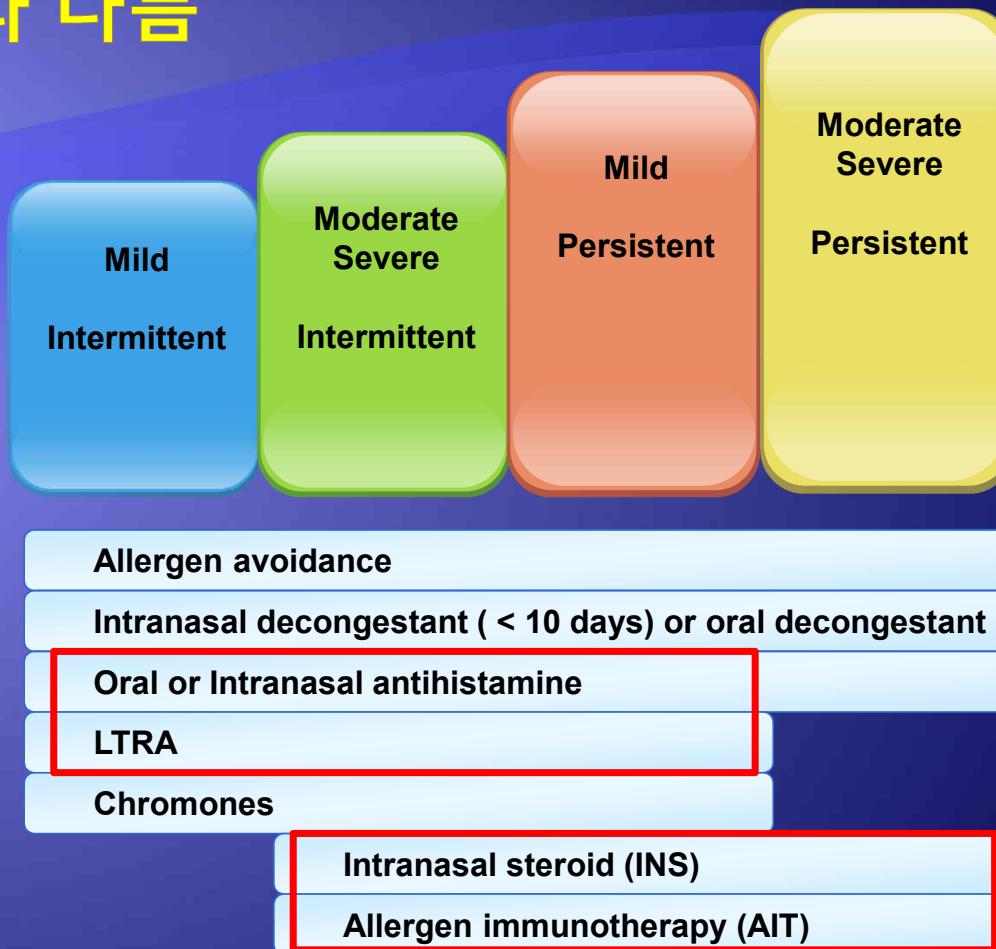
One or more

- Abnormal sleep
- Impairment of daily activities, sport, leisure
- Abnormal school and work
- Troublesome symptoms

Middleton 7th p 977

AR 치료: 중증도에 따라 다름

- 회피요법
- 약물요법
- 면역요법



Middleton 7th p 985

항히스타민제

- 히스타민 수용체: H1, H2, H3, H4
- 항히스타민제(inverse agonist): H1
 - ✓ 종류: 1세대, 2세대

1, 2세대 차이점

	1세대	2세대
BBB 통과	○	×
항콜린 효과	○	×

1세대/2세대 항히스타민제

Chemical class	1 st generation (old)	2 nd generation (new)
Alkylamines	Brompheniramine, chlorpheniramine, dimethindene, pheniramine, triprolidine	Acrivastine
Piperazines	Buclizine, cyclizine, hydroxyzine, meclizine, oxatomide	Cetirizine, levocetirizine
Piperidines	Azatadine, cyproheptatinde, diphenylpyraline, ketotifen	Astemizole, bepotastine, bilastine, desloratadine, ebastine, fexofenadine, levocabastine, loratadine, mizolastine, rupatadine, terfenadine, alcaftadine
Ethanolamines	Carbinoxamine, clemastine, dimenhydrinate, diphenhydramine, doxylamine, phenyltoloxamine	—
Ethylenediamines	Antazoline, pyrilamine, tripelennamine	—
Phenothiazines	Methdilazine, promethazine	—
Other	Doxepin	Azelastine, emedastine, epinastine, olopatadine

Middleton 8th, p1513
11

INS의 bioavailability 비교

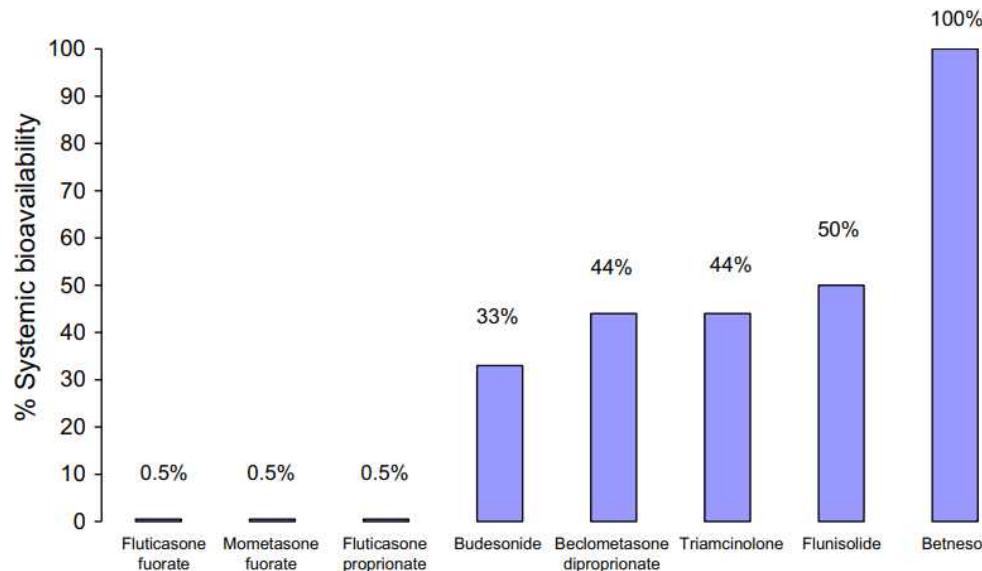
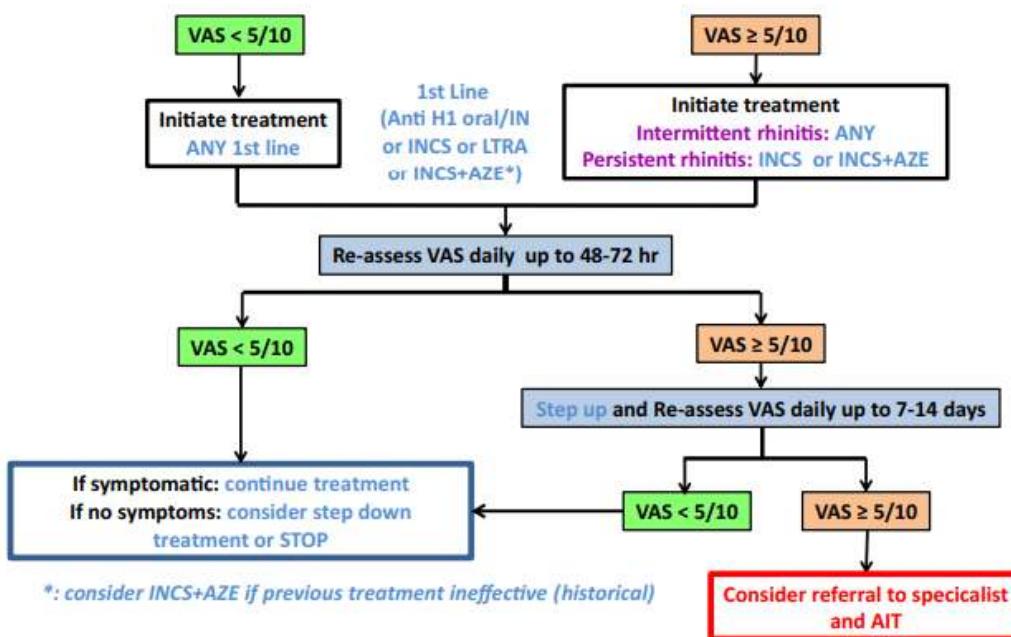


FIGURE 3 Bioavailability of intranasal corticosteroids. The more recent molecules have little systemic uptake and are suitable for use in children and for long-term therapy (Grade A evidence)

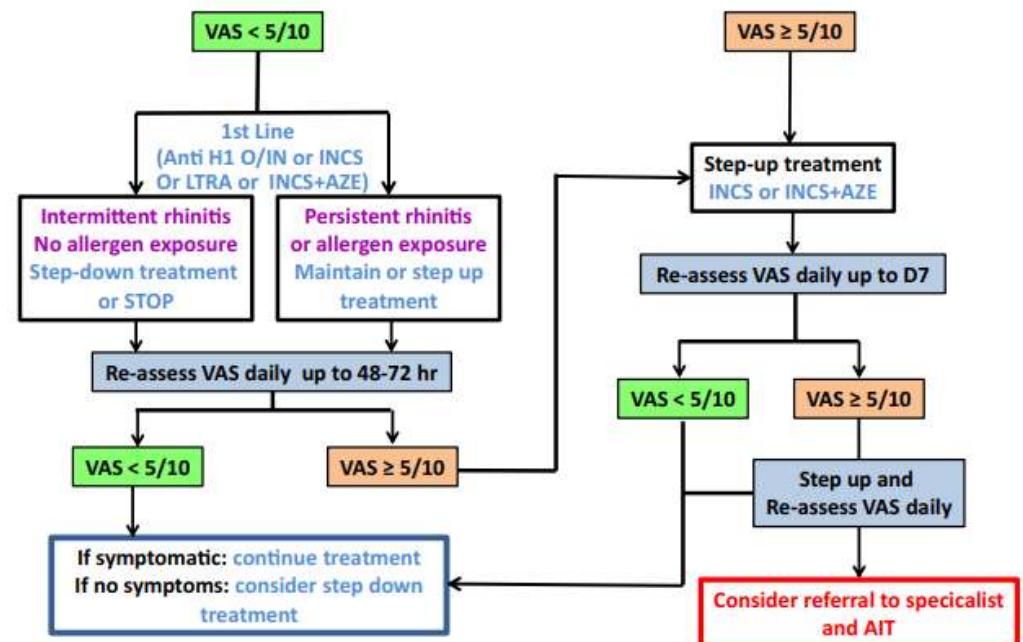
MACVIA clinical decision algorithm in adolescents and adults with allergic rhinitis



Assessment of control in untreated symptomatic patient



Assessment of control in treated symptomatic patient



**Next-generation Allergic Rhinitis and Its Impact
on Asthma (ARIA) guidelines for allergic rhinitis
based on Grading of Recommendations
Assessment, Development and Evaluation
(GRADE) and real-world evidence**

 Check for updates



**TABLE I. Classification of treatments used in patients with
allergic rhinitis⁶**

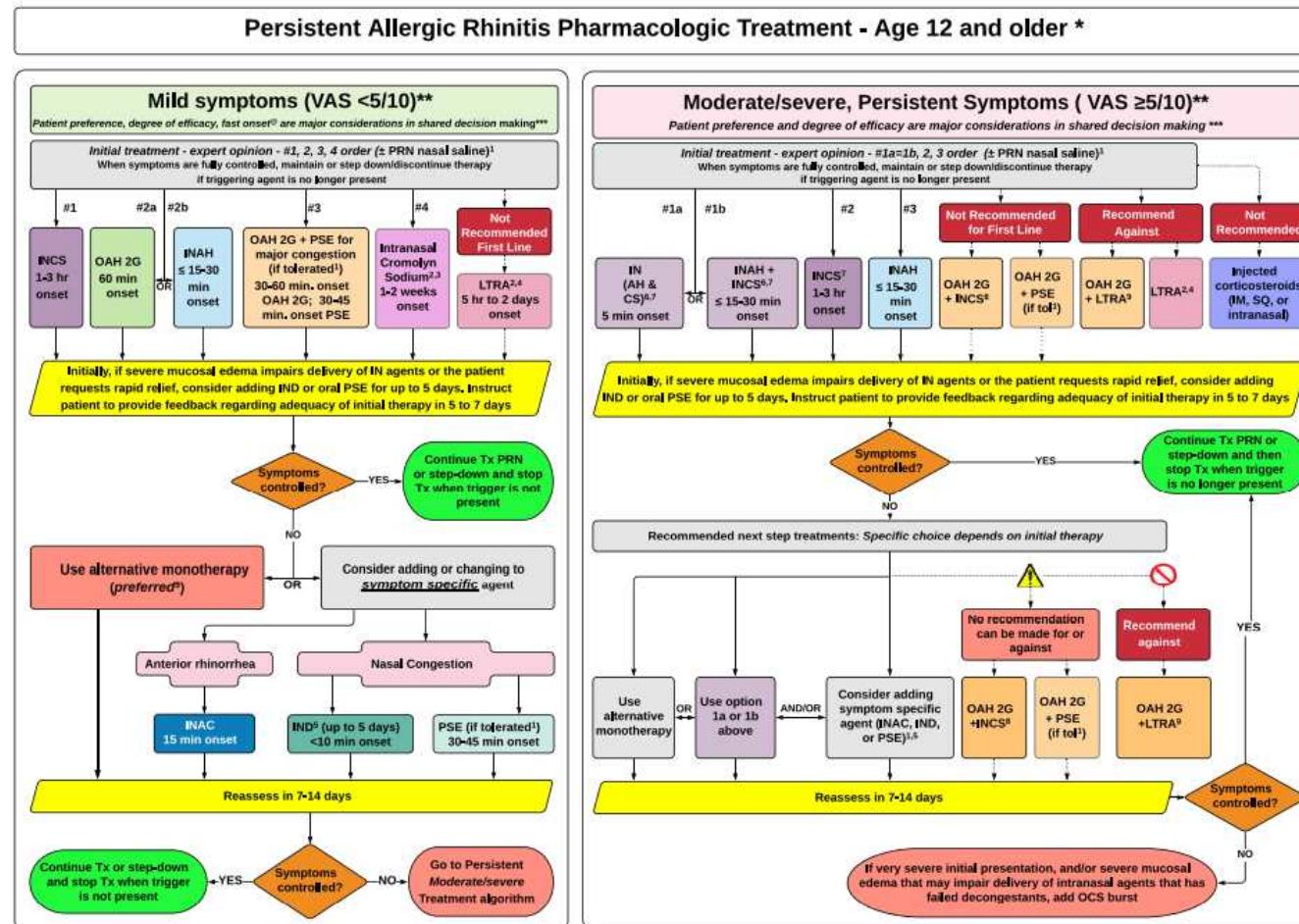
T1	Nonsedating H ₁ -antihistamine (oral, intranasal, and ocular), leukotriene receptor antagonists, or cromones (intranasal and ocular)
T2	INCSSs
T3	INCSSs + intranasal azelastine
T4	Oral corticosteroid as a short course and an add-on treatment
T5	Consider referral to a specialist and allergen immunotherapy

미국 지침

Practice parameter

Rhinitis 2020: A practice parameter update

 Check for updates



J Allergy Clin Immunol
2020;146:721-67

Table 1 | Treatment options for allergic rhinitis

Treatment	Rhinorrhoea	Sneezing	Nasal itch	Nasal obstruction	Ocular symptoms	Onset of action
Oral H ₁ -antihistamine	++	++	+	+	+	1–3 hours
Intranasal H ₁ -antihistamine	++	++	+	+	0	<30 minutes
Ocular H ₁ antihistamine	0	0	0	0	+++	15 minutes
Intranasal corticosteroid	+++	+++	+++	+++	+ to ++	6–48 hours
Intranasal corticosteroid plus intranasal H ₁ -antihistamine	++++	++++	++++	++++	+++	10–60 minutes
Nasal decongestant	0	0	0	+++	0	15 minutes
Intranasal chromone	+	+	+	+	0	15 minutes
Ocular chromone	0	0	0	0	++	15 minutes
Leukotriene receptor antagonist	+	+	+	+	0	1 hour
Intranasal anti-cholinergic agent	++	0	0	0	0	1 hour

0, no evidence of efficacy;+ to +++, increasing levels of evidence of efficacy.

INAH: 작용 시간 빠름

TABLE VIII. Onset of action of pharmacological agents for AR

Agent	Study design	Onset of action	Maximal effect	First measure of onset	References for onset	References for peak action
Intranasal steroid/antihistamine	EEU	5 min (azelastine/fluticasone propionate)	2 wk or greater	5 min	495	333
Intranasal decongestant-oxymetazoline	Peak nasal airflow	<10 min	? within an hour	10 min	496	
INAH	EEU	15 min (azelastine)	1 d to 4 wk	15 min	497,498	331,354
	EEU	30 min (olopatadine)	1 d to 4 wk	30 min	332,498,499	354
Intranasal anticholinergic	Methacholine challenge	15 min (ipratropium)	1 h	15 min	500	500
Oral antihistamine	EEU	30-90 min (desloratadine)		30 min	501	
	EEU	45 min (levocetirizine)		15 min	502	
	EEU	60 min (cetirizine)	1-8 d	15 min	497	503
	EEU	60-75 min (loratadine)	1-8 d	15 min	497,502,504	505
Oral antihistamine with decongestant	Single-dose park setting	30 min (loratadine/PSE)	Unknown	15 min	506	
INCS	EEU	1-6 h (ciclesonide)	2-4 wk	1 h	507,508	509
	EEU	2.5 h (mometasone)	4 wk	30 min	499	510
	EEU	3-8 h (budesonide)	2-4 wk	1 h	472,511	512,513
	2-wk seasonal study	8 h (fluticasone furoate)	2 wk	30 min	514	509,510,513
	Not EEU, park study or other	2-12 h (fluticasone propionate)	2-4 wk	2, 4, 12 h (meta-analysis)	515	512
LTRA	EEU	Within 5 h (montelukast)	By wk 2	5 h	516,517	518
Intranasal mast cell stabilizer	2-wk seasonal study	2 wk (cromolyn)	At least 2 wk	1 wk	435	435,519
Intranasal mast cell stabilizer before allergen exposure	EEU, nasal allergen challenge	Application 1-7 min before allergen exposure	N/A	≥10 min	442	N/A

EEU, Environmental exposure unit.

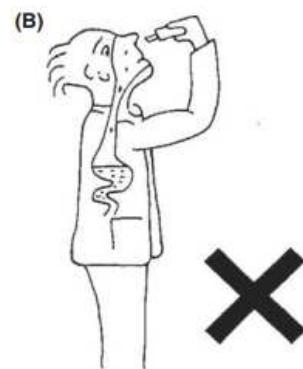
How to use a nasal spray and nasal drops

(A)

1. Shake bottle well
2. Look down
3. Using right hand for left nostril put nozzle just inside nose aiming towards outside wall
4. Squirt once or twice (2 different directions ↗ ↘)
5. Change hands and repeat for other side
6. Breathe in gently through the nose
7. Do not sniff



(B)



국내 비염 가이드라인

임상의를 위한 진료지침
알레르기비염

2022년 개정판

V 알레르기비염의 약물 치료

- 핵심질문 1
- 핵심질문 2
- 핵심질문 3
- 핵심질문 4

VI 알레르기비염의 비약물 치료

- 핵심질문 5
- 핵심질문 6
- 핵심질문 7
- 핵심질문 8
- 핵심질문 9
- 핵심질문 10



대한천식알레르기학회
The Korean Academy of Asthma, Allergy and Clinical Immunology

II 핵심질문과 권고안 요약

권고안

근거수준

권고등급

알레르기비염 환자에서 비강내 스테로이드/항히스타민제 병합요법은 비강내 스테로이드 단독요법보다 증상 완화에 더 효과적인가?

환자에게 비강내 스테로이드 단독요법과 비강내 스테로이드/항히스타민제 병합요법 중 하나를 선택*하여 치료할 수 있다.

*환자의 가치와 선호도, 이득과 위해를 고려한다.

Low

Conditional

알레르기비염 환자에서 비강내 스테로이드와 경구 항히스타민제 병합요법은 비강내 스테로이드 단독요법보다 증상 완화에 더 효과적인가?

환자에게 비강내 스테로이드 단독요법과 비강내 스테로이드와 경구 항히스타민제 병합요법 중 하나를 선택*하여 치료할 수 있다.

*환자의 가치와 선호도, 이득과 위해를 고려한다.

Low

Conditional

천식이 동반된 알레르기비염 환자에서 류코트리엔 수용체 길항제의 투여는 비염 증상을 완화시키고 비염치료제의 약물 요구량을 낮출 수 있는가?

천식이 동반된 알레르기비염 환자에서 비염 증상 개선을 위해 류코트리엔 수용체 길항제 사용을 선택*적으로 권고한다.

*환자의 가치와 선호도, 이득과 위해를 고려한다.

Low

Conditional

지속적 약물요법이 중요!

- 항히스타민제
- LTRA
- 비강내 스테로이드
- 시간이 지남에 따라 효과가 점점 더 나타남

비강내 azelastine, olopatadine

- 쓴맛(부작용) 미리 설명

AR과 NAR: 왜 구별해야 하는가?

- AR: 회피요법 + 면역요법 추가
- NAR: 경구 2세대 항히스타민제, LTRA 효과 부족

AR과 NAR: 약물 비교

	AR	NAR
경구 2세대 항히스타민제	○	×
경구 1세대 항히스타민제	○	○
비강내 항히스타민제	○	○
비강내 스테로이드	○	○
LTRA	○	×
혈관수축제(비강내, 경구)	○	○
항콜린제(비강내)	○	○

NAR: 비강내 항히스타민제?

- Intranasal azelastine
- 효과적 (코막힘도 호전)
- 작용 기전은?
 - ✓ 비점막에 고농도 약물 가능 → 항염증효과

신경펩티드 substance P

- 비강 azelastine 사용

NAR 환자군

✓ Substance P 감소

✓ Total rhinitis

symptoms scores

감소

Effect of intranasal azelastine on substance P release in perennial nonallergic rhinitis patients

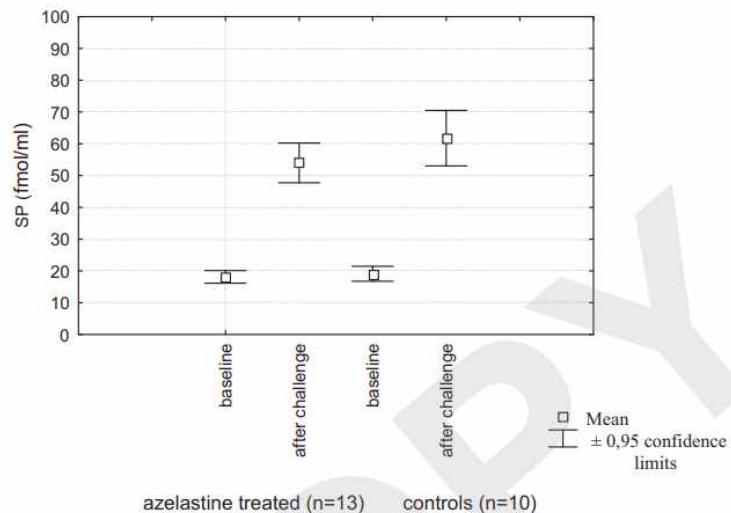
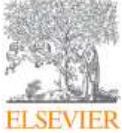


Figure 1. Concentration of substance P (SP) in nasal lavage fluid of non-allergic rhinitis (NAR) patients treated with azelastine (before and after saline challenge).



ORIGINAL ARTICLES

Efficacy of azelastine nasal spray in the treatment of vasomotor (perennial nonallergic) rhinitis

Charles H. Banov MD * , Phil Lieberman MD †, for the Vasomotor Rhinitis Study Groups ‡

Ann Allergy Asthma Immunol 2001;86:28-35

Original Article

Open-label evaluation of azelastine nasal spray in patients with seasonal allergic rhinitis and nonallergic vasomotor rhinitis

Phil Lieberman Michael A. Kaliner & William J. Wheeler
Pages 611-618 | Accepted 24 Feb 2005, Published online: 24 Apr 2005

<https://doi.org/10.1185/030079905X41408>

Curr Med Res Opin 2005;21:611-8

Review

Allergy Asthma Immunol Res. 2011 July;3(3):148-156.
doi: 10.4168/air.2011.3.3.148
pISSN 2092-7355 • eISSN 2092-7363



Management of Rhinitis: Allergic and Non-Allergic

Nguyen P Tran,¹ John Vickery,¹ Michael S Blaiss^{1,2*}

Antihistamines

Oral second generation antihistamines are not as effective in the treatment of NAR, though first generation oral antihistamines may have some benefit due to anticholinergic activity.³³

Topical antihistamines on the other hand have been found to be very effective for the overall treatment of NAR. Of the two topical antihistamines on the market in the United States (azelastine and olopatadine), azelastine is the only one that has been shown to be efficacious for nonallergic rhinitis.^{1,32,34} Banov

NAR: 비강내 스테로이드 역할

- 비염
 - ✓ AR과 NAR 모두 효과적
- 만성 부비동염
 - ✓ 급성 부비동염에도 효과적

INS + azelastine 복합제의 NAR 효과

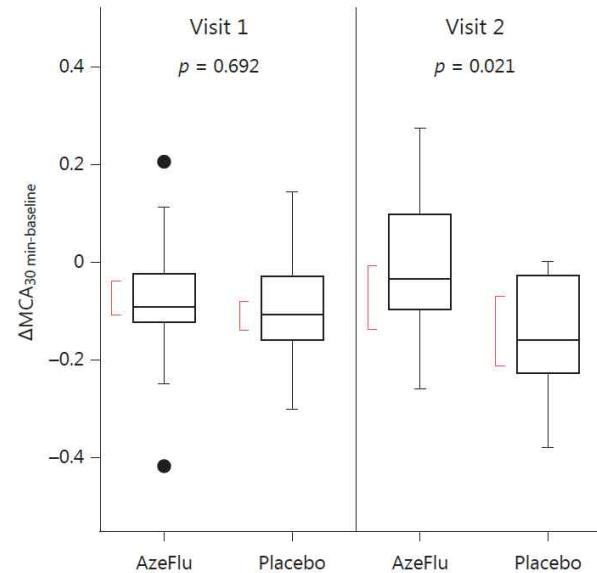
International Archives of
Allergy and
Immunology

Int Arch Allergy Immunol 2017;173:153–164
DOI: 10.1159/000478698

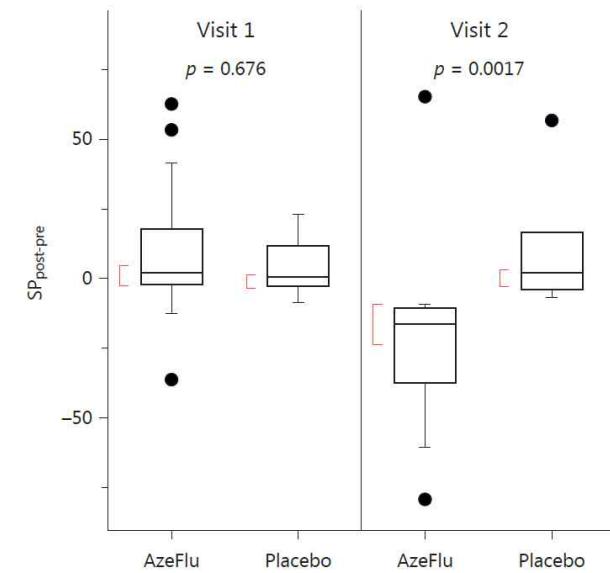
Received: December 5, 2016
Accepted after revision: June 13, 2017
Published online: August 9, 2017

A Pilot Study Investigating Clinical Responses and Biological Pathways of Azelastine/Fluticasone in Nonallergic Vasomotor Rhinitis before and after Cold Dry Air Provocation

찬공기 자극 코막힘 예방 비교



찬공기 자극 substance P 분비 비교



NAR: 그 외 방법들...

- 충혈제거제 (경구, 비강내)
- 항콜린제(비강내)
- LTRA: 효과 없음
- 비강내 capsaicin: 국내 없음
- 비강세척

비강세척(nasal irrigation)

- 생리식염수
- AR, NAR, 만성 부비동염
- Nasal spray보다 더 효과적
- 한 쪽 코에 200 mL 이상(Immunol Allergy Clin N Am 2016;36:305)

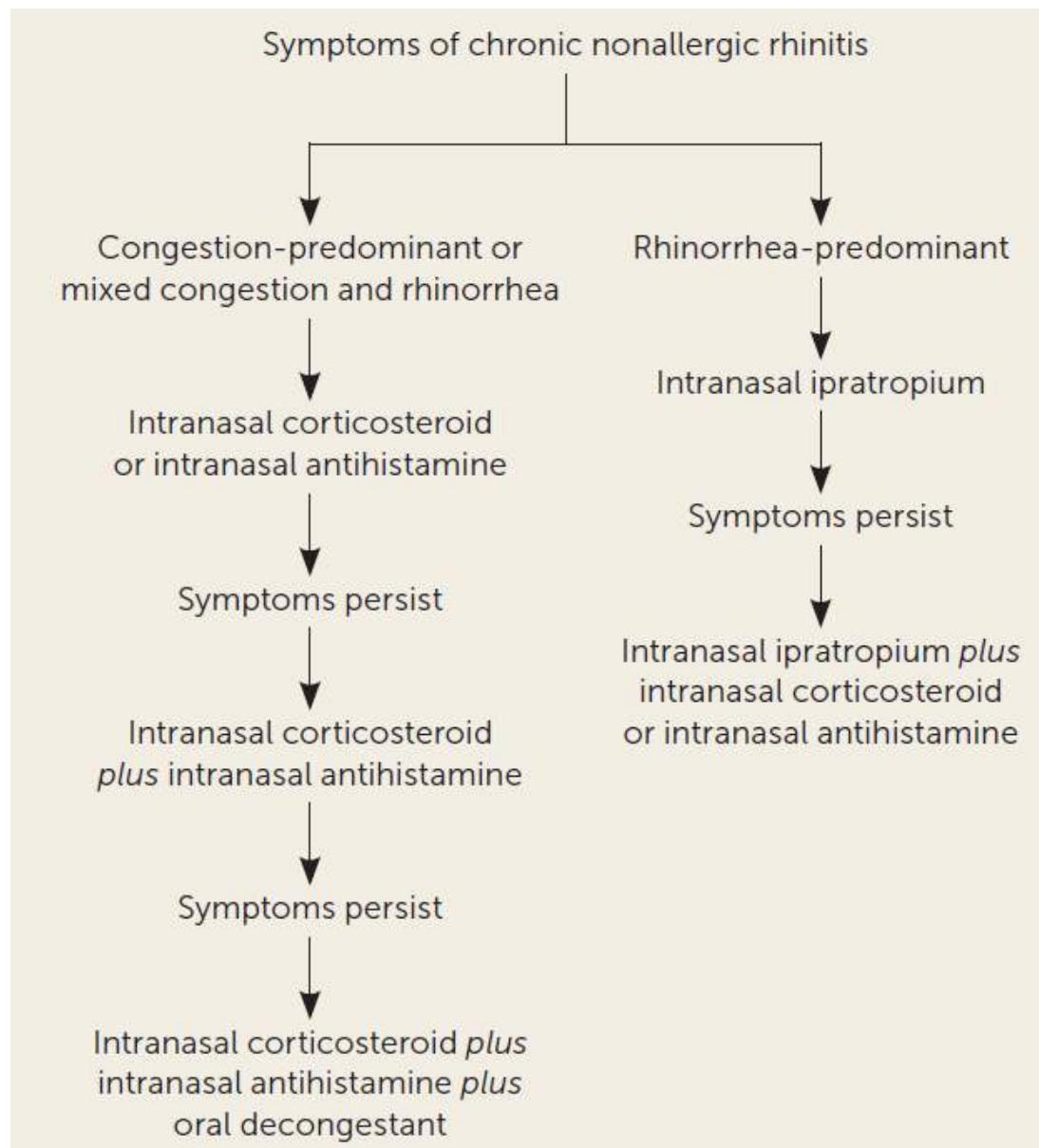
NAR: 약물치료 정리

- 비강내 azelastine ± 비강내 스테로이드 ± 비강내 항콜린제
- 경구약 추가
 - ✓ 콧물: 1세대 항히스타민제
 - ✓ 코막힘: 충혈제거제

WAO Journal 2009; 2:20

Algorithm for NAR treatment

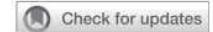
Am Fam Physician 2018;98:171



미국 NAR 지침

Practice parameter

Rhinitis 2020: A practice parameter update



Pharmacotherapy for NAR

Recommendation 32. CBS: We suggest that the clinician offer an INCS as a first-line therapy for NAR.

Strength of the recommendation: Conditional

Certainty of evidence: Low to moderate

Recommendation 33. CBS: We suggest that the clinician offer an INAH as a first-line therapy for NAR.

Strength of the recommendation: Conditional

Certainty of evidence: Very low

approved by the FDA for the treatment of SAR. Azelastine is also approved for the treatment of PAR and VMR.

toms of NAR.³⁴⁵ Although olopatadine has been demonstrated to significantly reduce nasal symptoms induced by a hyperosmolar mannitol challenge in patients with vasomotor NAR, there are no placebo-controlled trials to support its efficacy in relief of NAR symptoms.³⁴⁴

A randomized, double-blind, parallel-group, multicenter noninferiority study showed no significant difference between intranasal olopatadine and intranasal azelastine in controlling nasal symptoms in patients with nonallergic VMR.³⁵⁷ No significant

감기약 처방: 경구 항히스타민제?

- 50세 남자, 4일 전부터 콧물, 재채기, 코막힘, 기침, 가래, 목통증
호소
- 처방은?

주의할 점

- 비알레르기비염에서 국소알레르기비염 존재
 - ✓ 비알레르기비염 26.5%에서 국소알레르기비염
- 알레르기비염과 비알레르기비염 혼재
- 비강 내 구조적 질환 동반(부비동염, 비중격만곡)
 - ✓ 비내시경, 부비동 CT

정리



- AR과 NAR의 감별 필요 (왜?) **TABLE I. Classification of treatments used in patients with allergic rhinitis⁶**
- AR
 - ✓ 2세대 경구 항히스타민제
 - ✓ INAH → NAR 가능
 - ✓ LTRA
 - ✓ INS → NAR 가능
 - ✓ INS + INAH 복합제(조절이 안 되거나 심한 경우) → NAR 가능
- 1세대 경구 항히스타민제: NAR, 감기

T1	Nonsedating H ₁ -antihistamine (oral, intranasal, and ocular), leukotriene receptor antagonists, or cromones (intranasal and ocular)
T2	INCSs
T3	INCSs + intranasal azelastine
T4	Oral corticosteroid as a short course and an add-on treatment
T5	Consider referral to a specialist and allergen immunotherapy