2014 Asthma School

국내천식지침 및 GINA 2014

- 천식의 급성악화 -

2014. 9.27

서울의대, 서울특별시보라매병원 호흡기내과
김 덕 겸

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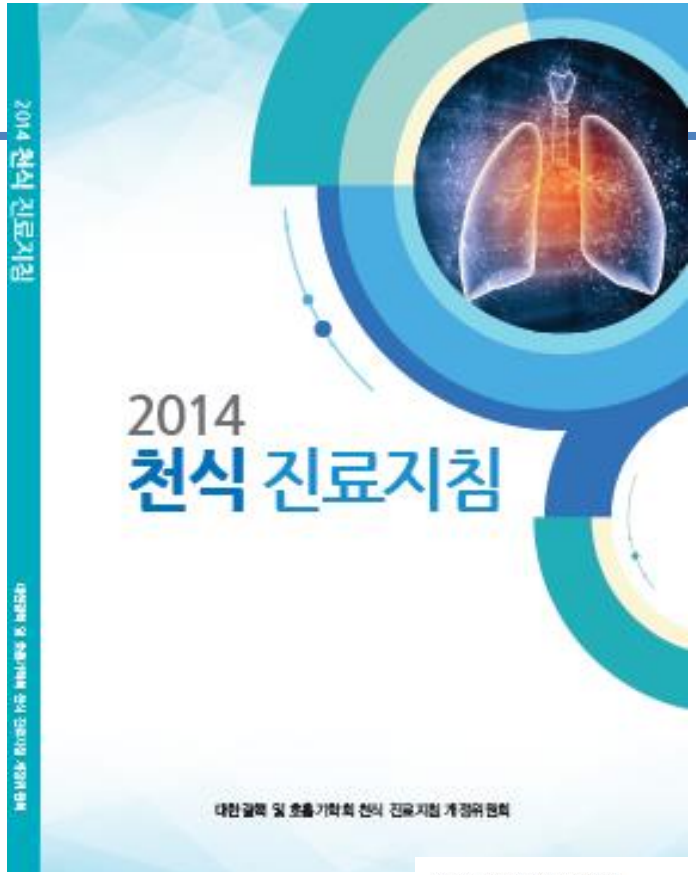
- 요약

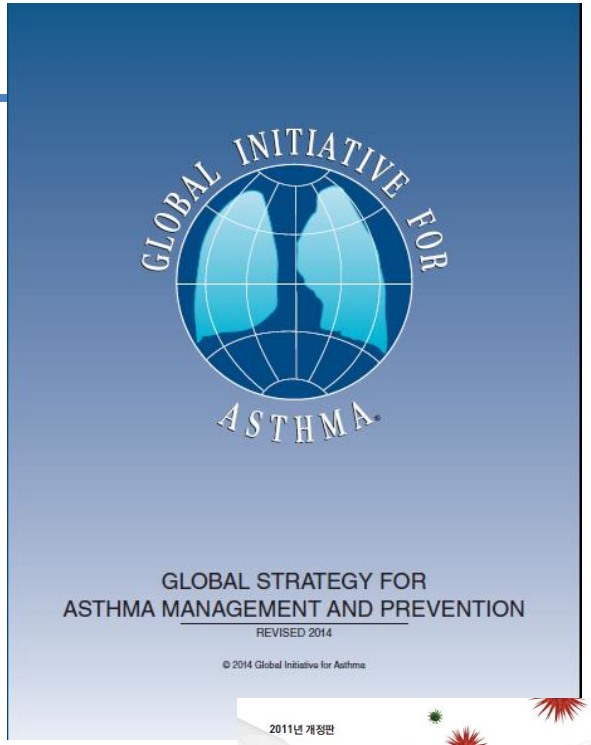
National Heart, Lung, and Blood Institute

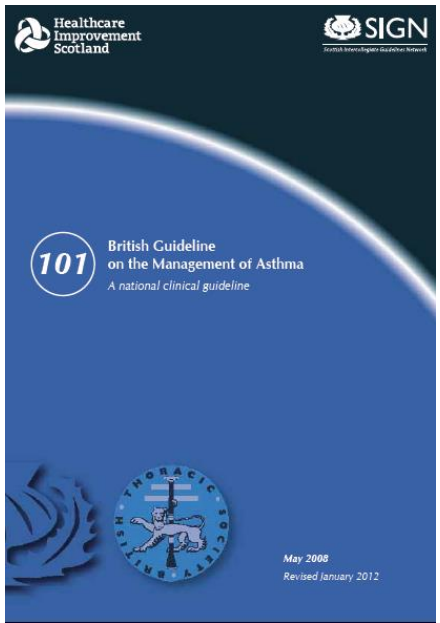
National Asthma Education and Prevention Program

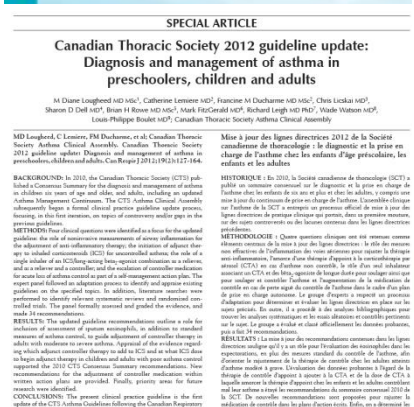
Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma

Full Report 2007



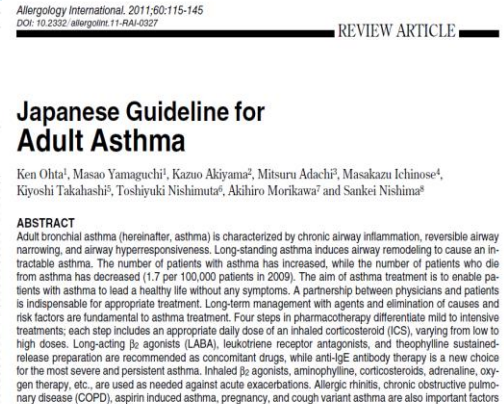





SPECIAL ARTICLE

Canadian Thoracic Society 2012 guideline update: Diagnosis and management of asthma in preschoolers, children and adults

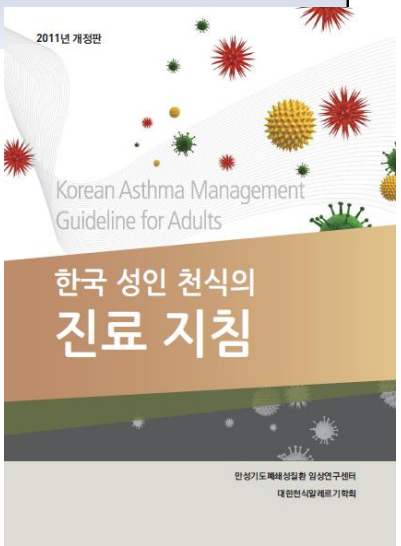
M Diane Lougheed MD MSc[1], Catherine Lemiere MD[2], Francine M Ducharme MD MSc[3], Chris Licskai MD[4], Sharon D Dell MD[4], Brian H Rowe MD MSc[5], Mark FitzGerald MD[6], Richard Leigh MD PhD[7], Wade Watson MD[8], Louis-Philippe Boulet MD[9], Canadian Thoracic Society Asthma Clinical Assembly


Allergology International. 2011;60:115-145
DOI: 10.2332/allergolint.11-RAI-0327

REVIEW ARTICLE

Japanese Guideline for Adult Asthma

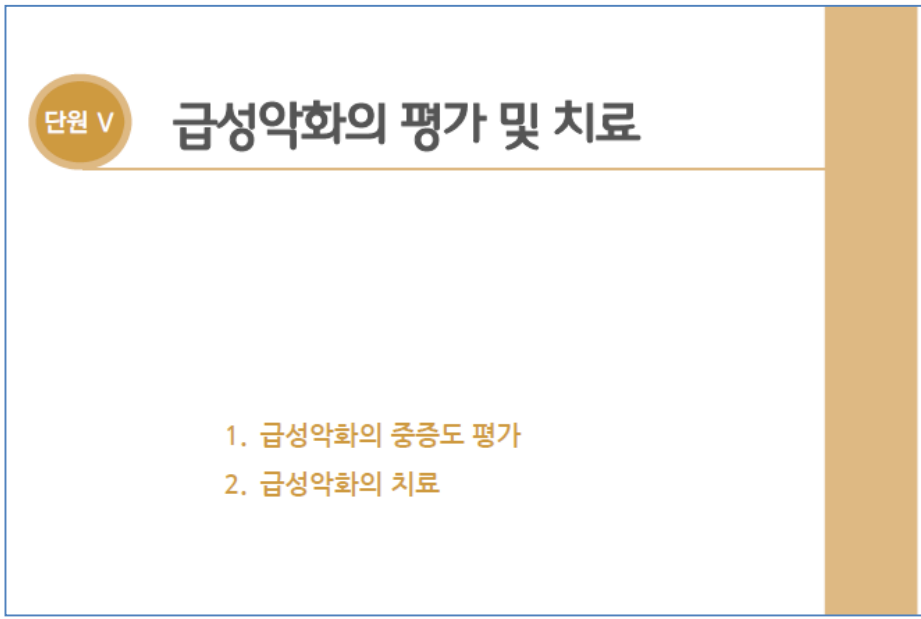
Ken Ohta[1], Masao Yamaguchi[1], Kazuo Akiyama[2], Mitsuru Adachi[3], Masakazu Ichinose[4], Kiyoshi Takahashi[5], Toshiyuki Nishimuta[6], Akihiro Morikawa[7] and Sankei Nishima[8]



TERMINOLOGY
DEFINITION

Chapter 4.

Management of worsening asthma and exacerbations



Terminology

- 급성악화, 천식 발작

- **Exacerbation**
  - commonly used in scientific and clinical literature
- Acute severe asthma
  - hospital-based studies
- **Flare-up**
  - Simpler, and conveys the sense that asthma is present even when symptoms are absent
- Attack
  - Various meaning, not perceived gradual worsening
- Episode
  - In pediatrics

Definition of "Exacerbation"

- Episodes characterized by **a progressive increase in symptoms** of shortness of breath, cough, wheezing or chest tightness and progressive **decrease in lung function**.

- *i.e.* they represent a change from the patient's usual status that is sufficient to require a change in treatment.

2014 GINA

Exacerbation

- GINA (2010)
  - "acute exacerbations" (asthma attacks or acute asthma)
  - "episodes of progressive increase in shortness of breath, cough, wheezing, or chest tightness, or some combination of these symptoms, accompanied by decreases in expiratory airflow that can be quantified by measurement of lung function"

"Exacerbation" appeared in other guidelines

- NAEPP EPR-3 (2007)
  - asthma exacerbations are *acute or subacute* episodes of progressively worsening shortness of breath, cough, wheezing, and chest tightness—or some combination of these symptoms". Exacerbations are characterized by decreases in expiratory airflow that can be documented and quantified by simple measurement of lung function (spirometry or PEF)

J Allergy Clin Immunol. 2012 March ; 129(3 Suppl): S34–S48

"Exacerbation" appeared in other guidelines

- ATS/ERS statement (2009)
  - events characterized by a change from the patient's previous status

- Severity
  - Severe
    - Use of systemic steroids
    - A hospitalization or emergency department
  - Moderate
    - Deterioration in symptoms
    - Deterioration in lung function
    - Increased use of short-acting β-agonist (SABA) bronchodilator

J Allergy Clin Immunol. 2012 March ; 129(3 Suppl): S34–S48

NIH-organized workshop

- **Exacerbation**
  - a worsening of asthma requiring the use of systemic corticosteroids (or for patients on a stable maintenance dose, an increase in the use of systemic corticosteroids) to prevent a serious outcome

- ***cf.*** **not well controlled asthma/uncontrolled asthma**
  - measures of chronic disease activity

Allergy Clin Immunol. 2012 March ; 129(3 Suppl): S34–S48

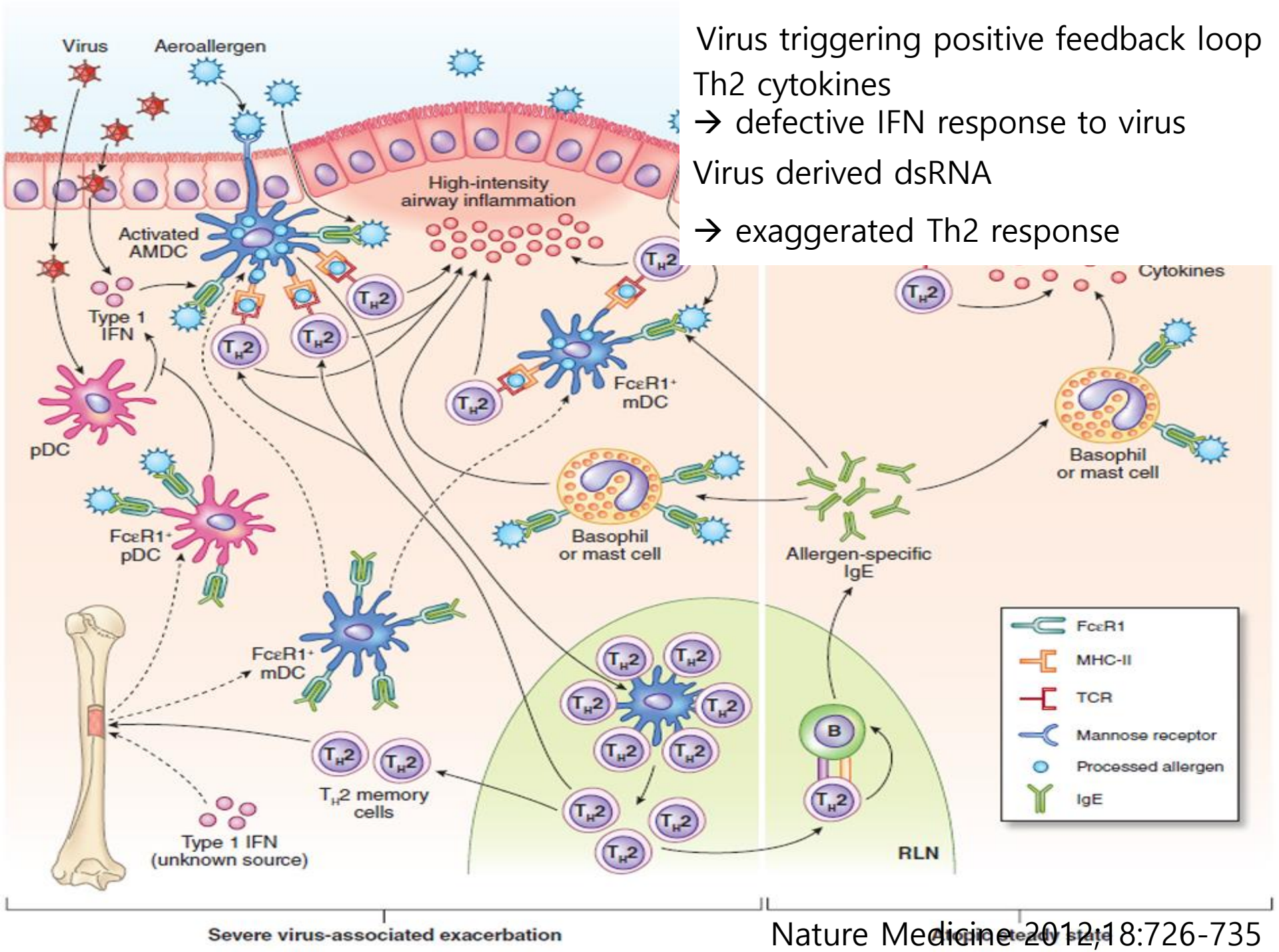
Virus triggering positive feedback loop

Th2 cytokines

→ defective IFN response to virus

Virus derived dsRNA

→ exaggerated Th2 response



Nature Medicine 2012;18:726-735

RISK FACTORS FOR EXACERBATION

Box 2-2. GINA assessment of asthma control in adults, adolescents and children 6–11 years

A. Asthma symptom control		Level of asthma symptom control		
In the past 4 weeks, has the patient had:		**Well controlled**	**Partly controlled**	**Uncontrolled**
• Daytime asthma symptoms more than twice/week?	Yes☐ No☐			
• Any night waking due to asthma?	Yes☐ No☐	None of these	1–2 of these	3–4 of these
• Reliever needed for symptoms* more than twice/week?	Yes☐ No☐			

Potentially modifiable independent risk factors for flare-ups (exacerbations)

- Uncontrolled asthma symptoms[68]
- Excessive SABA use (>1 x 200-dose canister/month)[69]
- Inadequate ICS: not prescribed ICS; poor adherence;[70] incorrect inhaler technique[71]
- Low FEV_1, especially if <60% predicted[72,73]
- Major psychological or socioeconomic problems[74]
- Exposures: smoking;[73] allergen exposure if sensitized[73]
- Comorbidities: obesity;[75] rhinosinusitis;[76] confirmed food allergy[77]
- Sputum or blood eosinophilia[78,79]
- Pregnancy[80]

Other major independent risk factors for flare-ups (exacerbations)

- Ever intubated or in intensive care unit for asthma[81]
- ≥1 severe exacerbation in last 12 months[82]

FEV_1: forced expiratory volume in 1 second; ICS: inhaled corticosteroid; OCS: oral corticosteroid; P450 inhibitors: cytochrome P450 inhibitors such as ritonavir, ketoconazole, itraconazole; SABA: short-acting $beta_2$-agonist.

*Excludes reliever taken before exercise. For children 6–11 years, also refer to Box 2-3. See Box 3-8, p38 for specific risk reduction strategies.

This consensus-based GINA control classification corresponds to that in GINA 2010–2012, except that lung function now appears only in the 'future risk' assessment. 'Current clinical control' has been renamed 'symptom control', to emphasize that these measures are not sufficient for assessment of disease control – future risk assessment for adverse outcomes is also needed. 'Independent' risk factors are those that are significant after adjustment for the level of symptom control. Poor symptom control and exacerbation risk should not be simply combined numerically, as they may have different causes and may need different treatment strategies.

Risk factors for flare-up (exacerbation)

Potentially modifiable independent risk factors	Other major independent risk factors
Uncontrolled asthma symptoms	Ever **intubated or ICU** for asthma
Excessive SABA use (> 1x200-dose canister/month)	**≥1 severe exacerbation** in last 12 months
Inadequate ICS -Not prescribed ICS -Poor adherence -Incorrect inhaler technique	
Low FEV1, especially if <60% predicted	
Major psychological or socioeconomic problems	
Exposures: smoking, sensitized allergen	
Comorbidities: obesity, rhnosinusitis, confirmed food allergy	
Sputum or blood **eosinophilia**	
Pregnancy	

천식악화의 위험인자

표 5-1. 천식악화의 위험인자

- 조절되지 않는 천식증상
- 과도한 흡입속효성베타작용제 사용(1달에 벤톨린 1개 이상 사용하는 경우)
- 부적절한 흡입스테로이드(ICS) 사용: 흡입스테로이드 처방을 하지 않은 경우, 약제 순응도가 나쁜 경우, 흡입기 사용이 부정확한 경우
- 폐기능이 나쁜 경우(특히, FEV_1 <60%)
- 흡연, 감작되어 있는 알레르겐에 노출된 경우
- 동반질환: 비만, 비염, 축농증, 확인된 음식 알레르기
- 객담 또는 혈액의 호산구증가증
- 임신
- 기관삽관 또는 중환자실에서 치료받은 천식악화가 있었던 경우
- 최근 12개월 이내에 1회 이상의 중증 악화를 경험한 경우

표 5-2. 천식 관련 사망을 높이는 인자

- 기관삽관과 인공호흡기 치료가 필요한 치명적인 천식악화 병력이 있는 경우
- 지난 1년 동안 천식 때문에 입원 또는 응급실 방문을 한 경우
- 전신스테로이드 현재 사용 중이거나 최근에 중단한 경우
- 흡입스테로이드를 사용하지 않는 경우
- 과도한 흡입속효성베타작용제 사용(한 달에 흡입속효성베타작용제 한 통 이상을 사용하는 경우)
- 정신과 질환이나 심리 사회적인 문제가 있는 경우
- 천식 약물과 문서화된 천식 행동지침에 순응도가 떨어지는 경우
- 음식 알레르기가 동반된 경우

Other demographic and environmental factors for AEBA

- Pediatric age >
- Female >
- Ethnicity
  - SES
  - Lower adherence
  - Disparities in the quality of healthcare
- Earlier age of onset
- Longer illness duration
- Genetic predisposition
  - *CHI3L1* (chitinase 3-like 1, YKL-40)
  - *ADRB2*
  - *FCER2*
  - *CRTAM*
  - *ORMDL3/GSDMB*
  - *IL4RA*

Curr Opin Allergy Clin Immunol 2013, 13:225–236

급성악화의 진단/평가

- Changes of symptoms
  - More sensitive measure of the onset of an exacerbation
- Quantification of lung function
  - More reliable indicators of severity in acute setting than symptoms

급성악화의 중증도 평가

- **병력청취**
  - 악화가 시작된 시점과 원인
  - 천식 증상의 중증도 평가
  - 아나필락시스 의심 증상
  - 천식 관련 사망인자 유무
  - 현재 사용 중인 증상완화제와 조절제
    - 용량, 흡입기 종류, 순응도, 최근 용량 변경 여부, 치료 반응 등 포함

- **신체검진**
  - 중증 발작의 징후와 활력 징후
    - 의식, 체온, 맥박수, 호흡 수, 혈압, 문장 구사 능력, 호흡보조근 사용, 천명음 등
  - 악화인자
    - 아나필락시스, 폐렴, 기흉 등
  - 급성 호흡곤란을 일으킬 수 있는 다른 질환의 징후
    - 심부전, 상기도 폐쇄, 이물질 흡입, 폐색전증 등

- **객관적 측정 지표**
  - 산소포화도
  - 최대호기유량

급성악화의 중증도 평가

- 1차 의료기관에서의 중증도 평가
  - **병력청취**
  - **신체검진**
  - 객관적 검사

- 응급실에서의 중증도 평가
  - 병력청취
  - 신체검진
  - **객관적 검사**
    - **폐기능검사** :
      - 치료의 지체를 초래하지 않는다면 **치료 시작 전에** 최대호기유량이나 FEV1을 측정
      - **치료에 대해 뚜렷한 반응이 있거나 더 이상 반응이 없을 때까지** 시간 간격을 두고 측정
    - **산소포화도:**
      - 산소가 투여되기 전에 측정, 환자가 안정이 되면 산소 투여 중단 5분 후에 측정
    - **ABGA**
      - 초기 치료에도 불구하고 최대호기유량이나 FEV1이 예측치의 50% 미만
      - 초기 치료에 반응을 하지 않거나 환자 상태가 악화가 될 때
    - **흉부X선**

Figure 8. Severity of Asthma Exacerbations*

Parameter	Mild	Moderate
Breathless	Walking Can lie down	Talking Infant - softer, short difficulty feeding Prefer sitting
Talks in	Sentences	Phrases
Alertness	May be agitated	Usually agitated
Respiratory rate	Increased	Increased
		Normal rates of breathing in
SaO_2% (on air)†	>95%	91 - 95%
		Hypercapnia (hyperventilation) develops more readily in

*Note: The presence of several parameters, but not necessarily all, indicates t
†Note: Kilopascals are also used internationally, conversion would be appropr

표 4.4-1. 급성 발작의 중증도 분류

	경증	중등증	중증	치명적 발작
호흡곤란	보행 시 호흡곤란 누울 수 있음	누으면 호흡곤란 주로 앉아 있음	휴식 시 호흡곤란 앞으로 구부리고 있음	
말하기	문장으로 구사 가능	구절로만 구사	단어로 구사	
경적능이 있을 수 있음				
$PaCO_2$	<45mmHg	<45mmHg	>45mmHg	
SaO_2	>95%	91-95%	<90%	

ASSESS the PATIENT

Is it asthma?

Risk factors for asthma-related death? *(Box 4-1)*

Severity of exacerbation?

MILD or MODERATE

Talks in phrases, prefers sitting to lying, not agitated

Respiratory rate increased

Accessory muscles not used

Pulse rate 100–120 bpm

O_2 saturation (on air) 90–95%

PEF >50% predicted or best

SEVERE

Talks in words, sits hunched forwards, agitated

Respiratory rate >30/min

Accessory muscles in use

Pulse rate >120 bpm

O_2 saturation (on air) <90%

PEF ≤50% predicted or best

LIFE-THREATENING

Drowsy, confused or silent chest

URGENT

한국성인천식의 진료지침2011

급성악화의 평가/중증도

표 5-3. 천식 급성악화 환자 평가

경증 또는 중등증	중증	치명적 발작
문장으로 말할 수 있음	단어로 말함	
눕는 것 보다는 앉는 것을 선호	앞으로 구부리고 앉아 있음	
불안해 하지 않음	불안해 함	
호흡수 증가	호흡수: >30회/분	의식 장애
호흡보조근 사용하지 않음	호흡보조근 사용함	호흡음 소실
맥박수: 100~120회/분	맥박수: >120회/분	
산소포화도(실내공기): 90~95%	산소포화도(실내공기): <90%	
최대호기유량: >50% (예측치 또는 개인 최고치)	최대호기유량: ≤50% (예측치 또는 개인 최고치)	

MANAGEMENT OF ASTHMA EXACERBATION

1. SELF MANAGEMENT WITH ACTION PLAN → 환자 행동지침
2. IN PRIMARY CARE
3. IN EMERGENCY DEPARTMENT

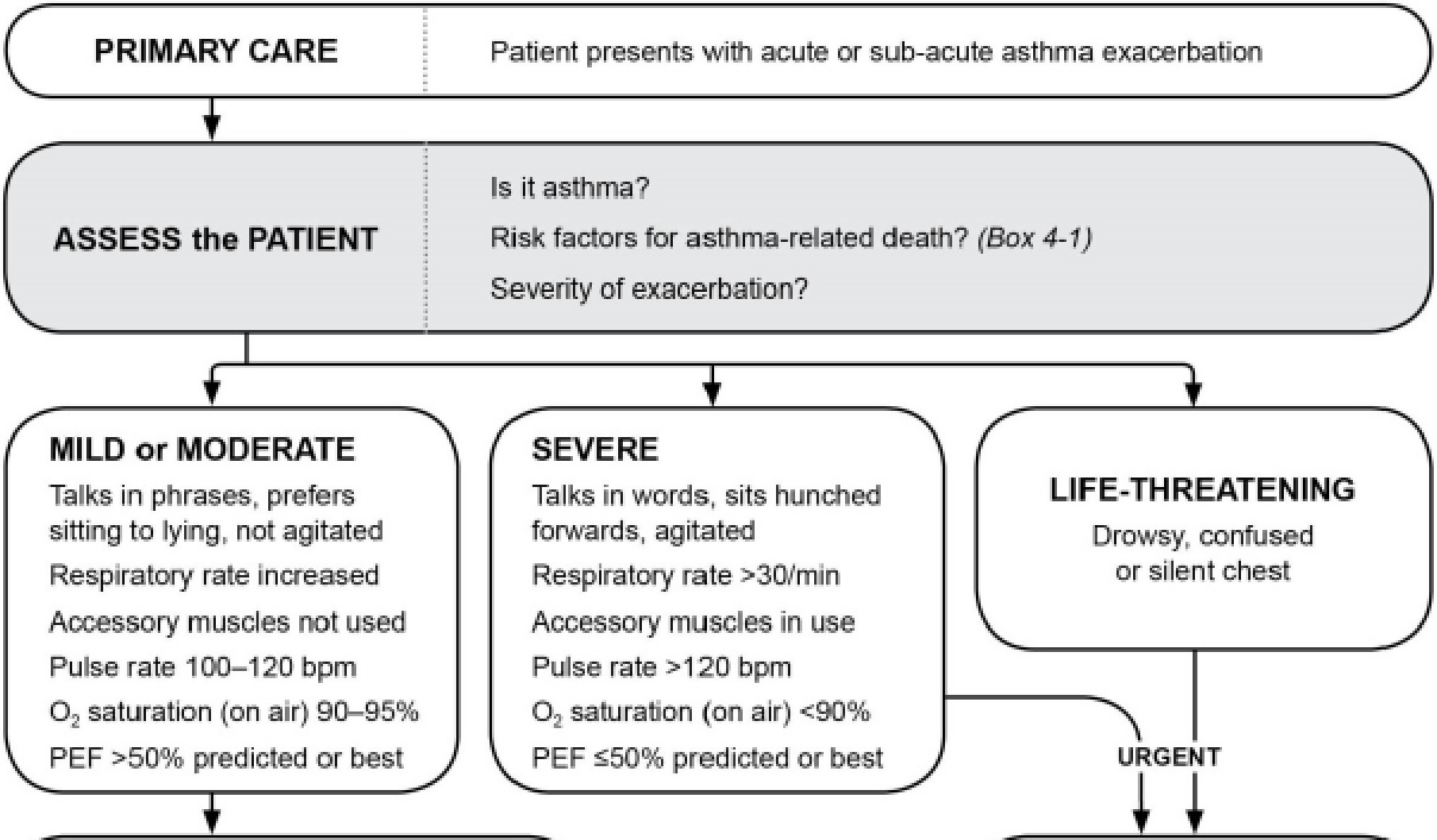
1. 1차 의료기관에서의 치료
2. 병원 응급실 치료

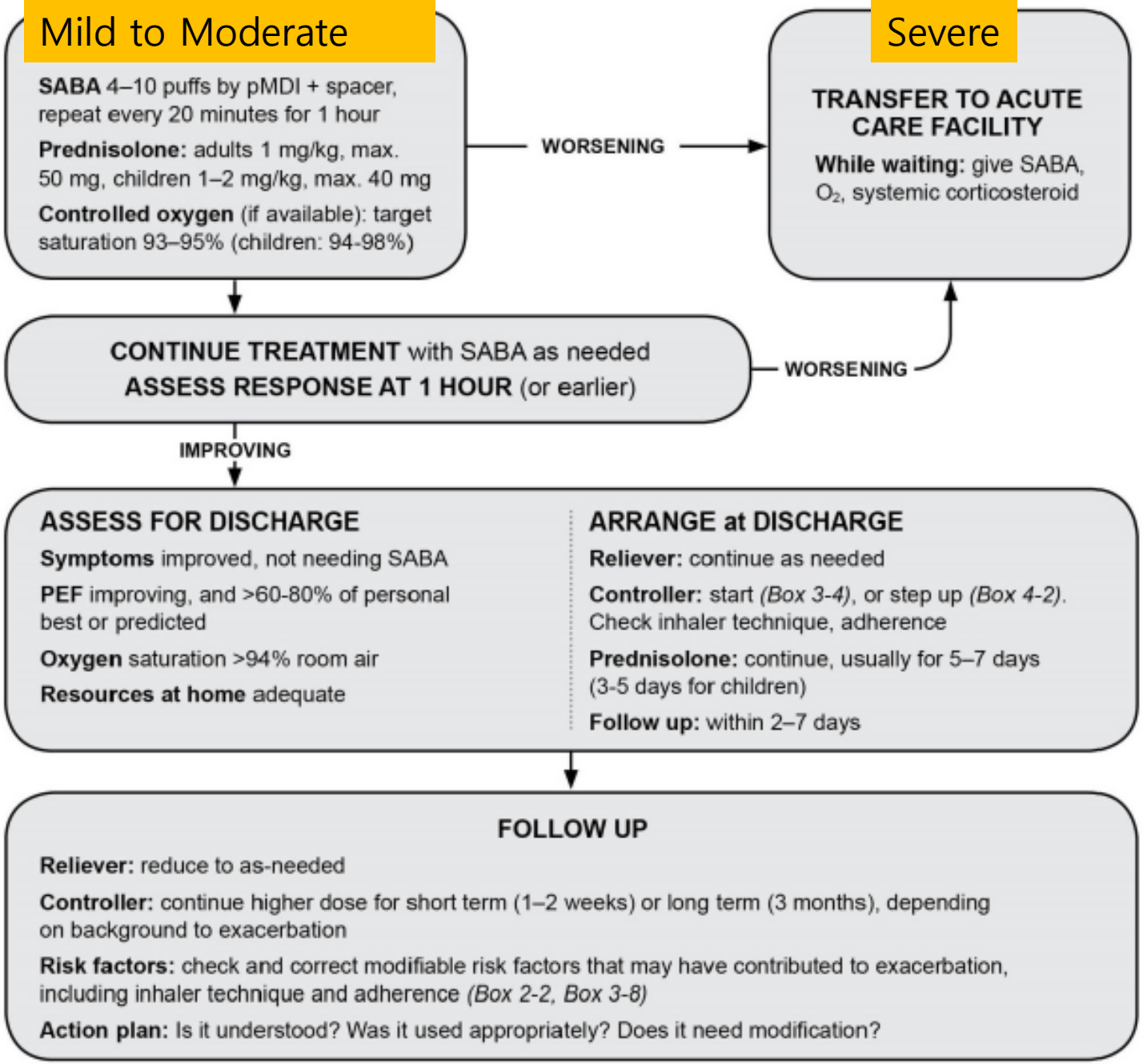
급성악화 시 행동지침

표 7-6. 행동지침

치료약	악화 동안 1-2주 단기 변화
증상완화제 증량	
SABA	SABA의 빈도를 증가 MDI인 경우 흡입보조기 사용
저용량 ICS/formoterol 조절제 증량	증상완화제의 사용을 증가(formoterol 기준으로 최대 72 ㎍/일)
조절제 증량	
ICS/formoterol을 조절제와 증상완화제로 사용	조절제는 유지하고 증상완화제를 필요 시 증량(formoterol 기준으로 최대 72 ㎍/일)
ICS를 조절제, SABA를 증상완화제로 사용	최소 ICS를 두 배로 올리고 최대 용량까지 올릴 것을 고려(beclomethasone 기준 최대 2,000 ㎍/일)
ICS/formoterol을 조절제, SABA를 증상완화제로 사용	조절제를 4배로 증량(formoterol 기준으로 최대 72 ㎍/일)
ICS/salmeterol을 조절제, SABA를 증상완화제로 사용	조절제를 더 높은 용량으로 높이거나 단독 ICS 흡입기 추가(beclomethasone 기준 최대 2,000 ㎍/일)
경구스테로이드제를 추가하고 의사에게 연락	
Prednisolone	심한 악화 (최대호기유량이나 FEV_1<개인 최대치의 60%) 또는 치료에도 호전되지 않으면 prednisolone 1 mg/kg/일(최대 50 mg, 5~7일 동안 사용, 2주 미만 사용은 바로 끊는다.)

In primary care

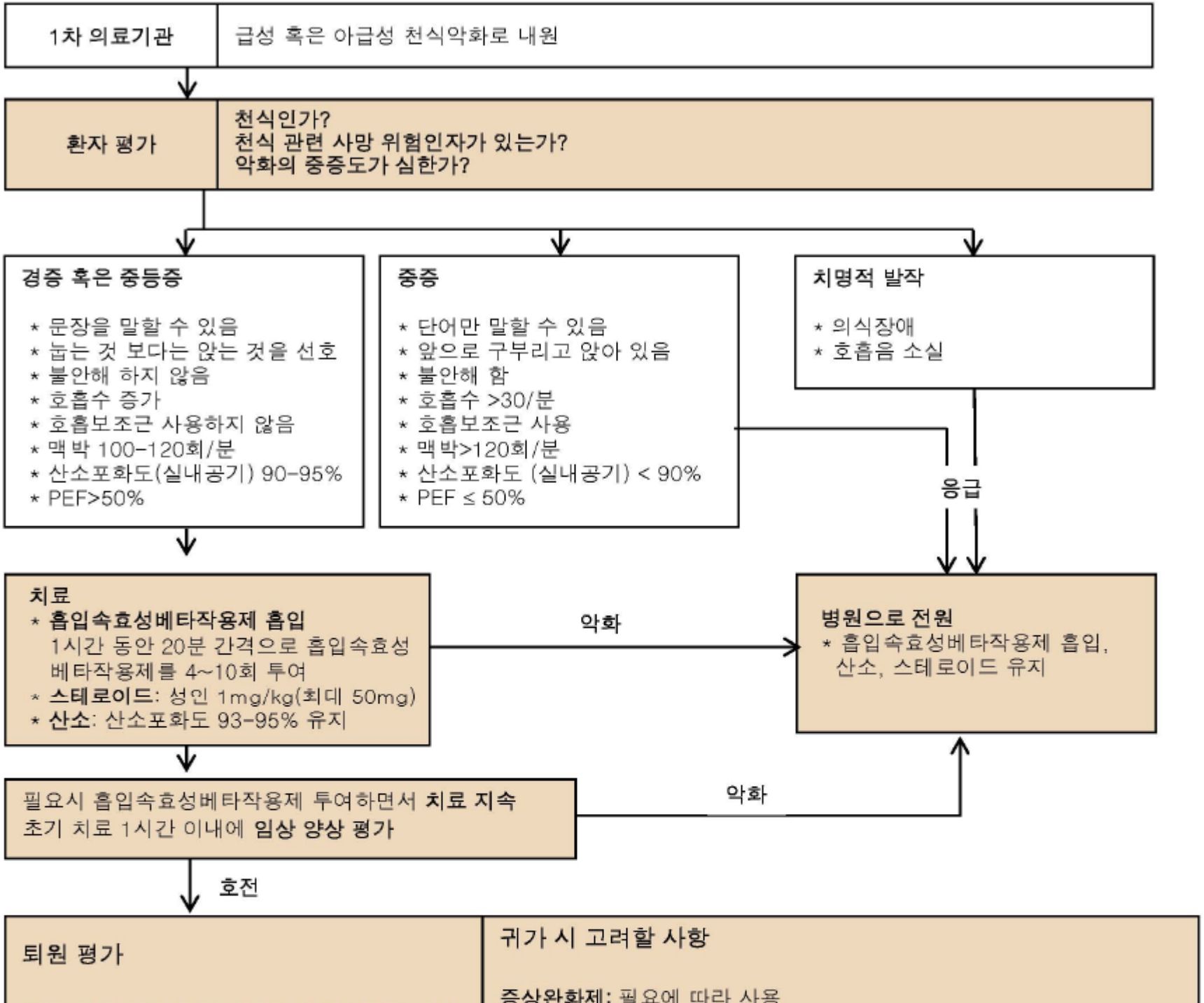



Mild to Moderate
SABA 4–10 puffs by pMDI + spacer, repeat every 20 minutes for 1 hour
Prednisolone: adults 1 mg/kg, max. 50 mg, children 1–2 mg/kg, max. 40 mg
Controlled oxygen (if available): target saturation 93–95% (children: 94-98%)
WORSENING
Severe
TRANSFER TO ACUTE CARE FACILITY
While waiting: give SABA, O2, systemic corticosteroid
CONTINUE TREATMENT with SABA as needed
ASSESS RESPONSE AT 1 HOUR (or earlier)
WORSENING
IMPROVING
ASSESS FOR DISCHARGE
Symptoms improved, not needing SABA
PEF improving, and >60-80% of personal best or predicted
Oxygen saturation >94% room air
Resources at home adequate
ARRANGE at DISCHARGE
Reliever: continue as needed
Controller: start (Box 3-4), or step up (Box 4-2). Check inhaler technique, adherence
Prednisolone: continue, usually for 5–7 days (3-5 days for children)
Follow up: within 2–7 days
FOLLOW UP
Reliever: reduce to as-needed
Controller: continue higher dose for short term (1–2 weeks) or long term (3 months), depending on background to exacerbation
Risk factors: check and correct modifiable risk factors that may have contributed to exacerbation, including inhaler technique and adherence (Box 2-2, Box 3-8)
Action plan: Is it understood? Was it used appropriately? Does it need modification?

Initial management of AE

- **At primary Care**
  - SABA
    - 4-10puff q 20min for 1hr
  - Controlled oxygen therapy
    - 93-95%
  - Systemic corticosteroids
    - 1mg/kg/day, ~50mg/d
    - 5-7days
  - Controllers
    - advice about increasing the dose for the next 2–4 weeks
  - Antibiotics
    - Not recommended

- **At ER**
  - oxygen Tx.
    - 93-95%
  - SABA
    - pMDI + spacer
    - Continuous > intermittent
  - Systemic corticosteroids
    - 1mg/kg/day, ~50mg/dx5-7days
      - Failed initial SABA
      - AE while taking OCS
      - Hx of AE requiring OCS
  - ICS
    - High dose of ICS in pts not receiving OCS
  - Others
    - Ipratropium
    - Theophylline
    - Mg
    - LTRA
    - ICS/LABA
    - Antibiotics
    - NIV


1차 의료기관
급성 혹은 아급성 천식악화로 내원
환자 평가
천식인가?
천식 관련 사망 위험인자가 있는가?
악화의 중증도가 심한가?
경증 혹은 중등증
* 문장을 말할 수 있음
* 눕는 것 보다는 앉는 것을 선호
* 불안해 하지 않음
* 호흡수 증가
* 호흡보조근 사용하지 않음
* 맥박 100-120회/분
* 산소포화도(실내공기) 90-95%
* PEF>50%
중증
* 단어만 말할 수 있음
* 앞으로 구부리고 앉아 있음
* 불안해 함
* 호흡수 >30/분
* 호흡보조근 사용
* 맥박>120회/분
* 산소포화도 (실내공기) < 90%
* PEF ≤ 50%
치명적 발작
* 의식장애
* 호흡음 소실
응급
치료
* 흡입속효성베타작용제 흡입
1시간 동안 20분 간격으로 흡입속효성 베타작용제를 4~10회 투여
* 스테로이드: 성인 1mg/kg(최대 50mg)
* 산소: 산소포화도 93-95% 유지
악화
병원으로 전원
* 흡입속효성베타작용제 흡입, 산소, 스테로이드 유지
필요시 흡입속효성베타작용제 투여하면서 치료 지속
초기 치료 1시간 이내에 임상 양상 평가
악화
호전
퇴원 평가
귀가 시 고려할 사항
증상완화제: 필요에 따라 사용

SABA

- Rapic
  - G
  - K
- Deliv
  - **p**
  - 효과
  - S

Study or Subgroup	Holding Chamber Events	Total	Nebuliser Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 Adults						
Colacone 1993	1	40	0	40	1.5%	3.00 [0.13, 71.51]
Dhuper 2008	1	29	2	29	6.1%	0.50 [0.05, 5.21]
Idris 1993	1	15	1	20	2.6%	1.33 [0.09, 19.64]
Raimondi 1997	0	9	0	9		Not estimable
Rao 2002	0	25	1	25	4.6%	0.33 [0.01, 7.81]
Rodrigo 1993	5	49	4	48	12.3%	1.22 [0.35, 4.29]
Rodriguez 1999	14	36	17	33	54.0%	0.75 [0.45, 1.28]
Turner 1988	4	27	5	26	15.5%	0.77 [0.23, 2.56]
Vivek 2003	5	68	1	54	3.4%	3.97 [0.48, 32.98]
Subtotal (95% CI)		**298**		**284**	**100.0%**	**0.94 [0.61, 1.43]**
Total events	31		31			
Heterogeneity: Chi² = 3.99, df = 7 (P = 0.78); I² = 0%						
Test for overall effect: Z = 0.29 (P = 0.77)						
1.1.2 Children						
Chong-Neto 2005	0	20	0	10		Not estimable
Chou 1995	4	71	5	81	11.4%	0.91 [0.25, 3.27]
Direkwatanachai 2008	1	68	2	77	4.6%	0.57 [0.05, 6.11]
Jamalvi 2006	4	84	7	66	19.1%	0.45 [0.14, 1.47]
Leversha 2000	10	30	18	30	43.8%	0.56 [0.31, 1.00]
Ploin 2000	3	31	3	32	7.2%	1.03 [0.23, 4.73]
Sannier 2007	6	39	3	40	7.2%	2.05 [0.55, 7.63]
Vazquez 1992	0	9	0	9		Not estimable
Williams 1996	2	42	2	18	6.8%	0.43 [0.07, 2.81]
Subtotal (95% CI)		**394**		**363**	**100.0%**	**0.71 [0.47, 1.08]**
Total events	30		40			
Heterogeneity: Chi² = 4.45, df = 6 (P = 0.62); I² = 0%						
Test for overall effect: Z = 1.61 (P = 0.11)						
Test for subgroup differences: Chi² = 0.85, df = 1 (P = 0.36), I² = 0%						

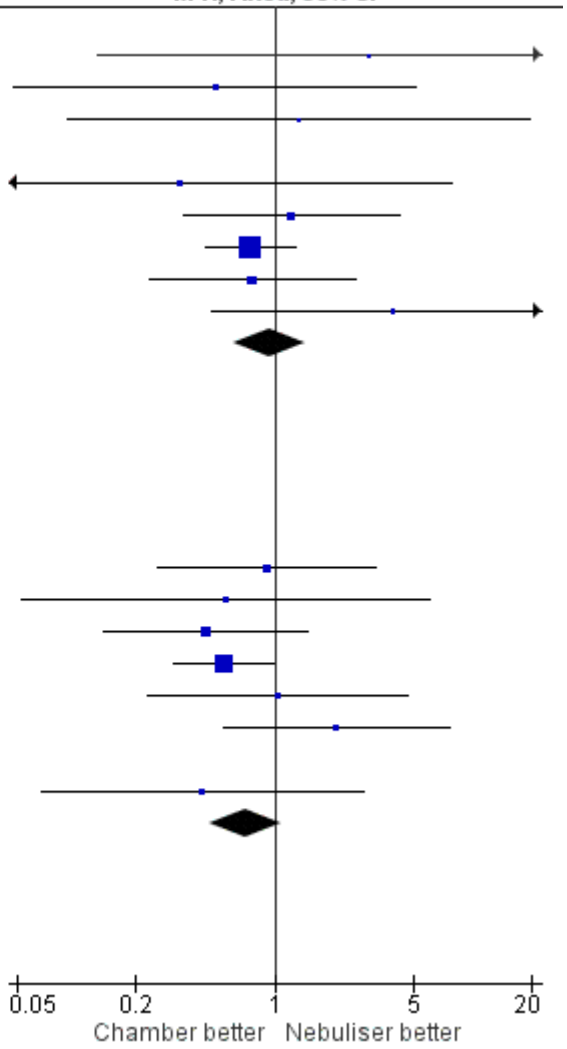
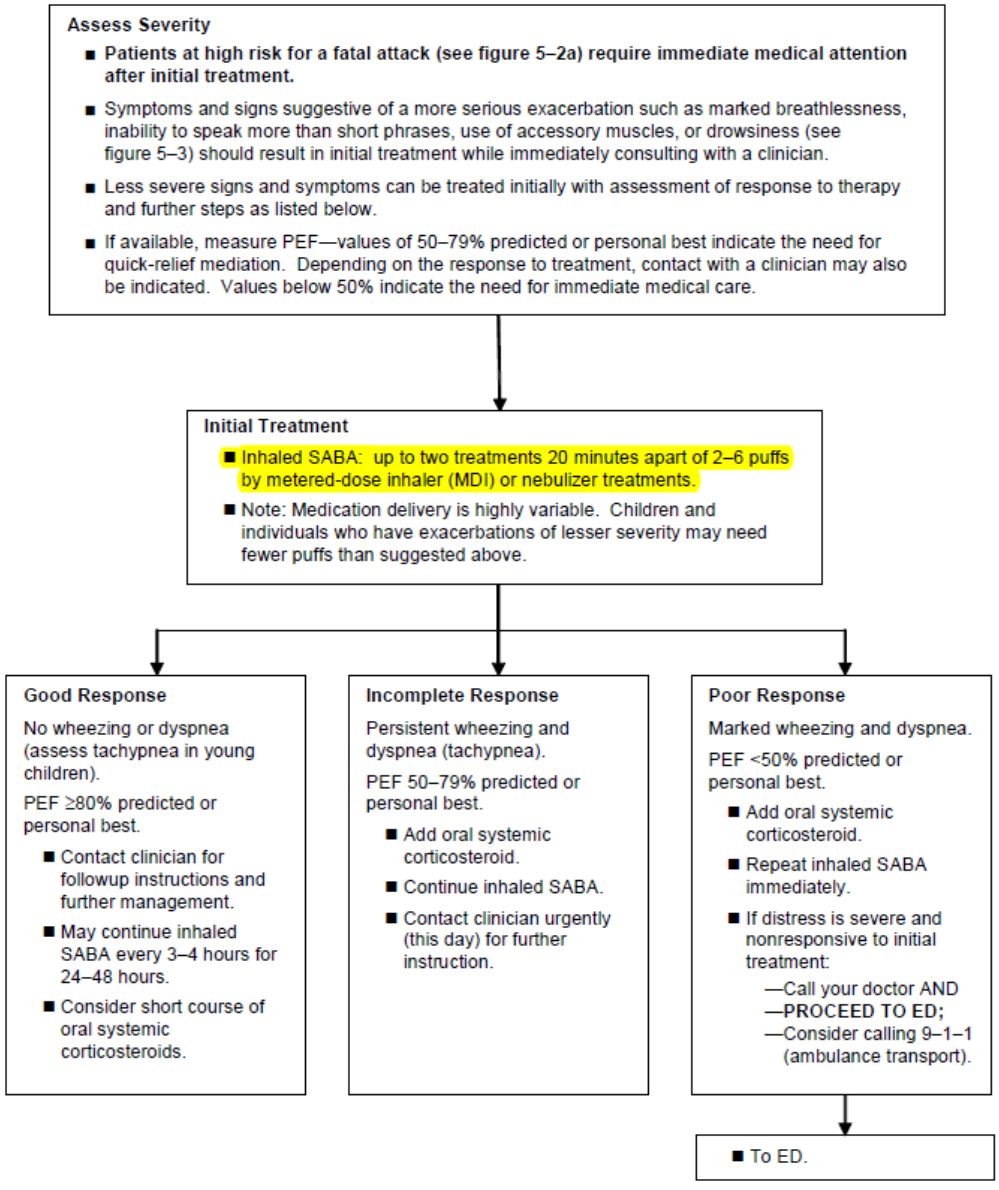


FIGURE 5–4. MANAGEMENT OF ASTHMA EXACERBATIONS: HOME TREATMENT



NAEPP 2007

Comparison 1. Any steroid (po, IM, IV, inhaled) vs placebo

Outcome	No. of Studies	No. of Participants	Statistical method	Effect size
Admitted to hospital (all times)	12	844	Odds Ratio (M-H, Random, 95% CI)	0.50 [0.31, 0.81]
Admitted to hospital (1-2 hours)	2	126	Odds Ratio (M-H, Random, 95% CI)	1.38 [0.41, 4.67]
Admitted to hospital (3-4 hours)	6	366	Odds Ratio (M-H, Random, 95% CI)	0.47 [0.24, 0.91]
Admitted to hospital (5-6 hours)	7	606	Odds Ratio (M-H, Random, 95% CI)	0.31 [0.15, 0.64]

Comparison 2. Route of administration (Admission)

Outcome	No. of Studies	No. of Participants	Statistical method	Effect size
IV vs placebo	7	529	Odds Ratio (M-H, Random, 95% CI)	0.68 [0.39, 1.21]
Oral vs Placebo	4	291	Odds Ratio (M-H, Random, 95% CI)	0.24 [0.11, 0.53]

Comparison 6. Population

Outcome	No. of Studies	No. of Participants	Statistical method	Effect size
Asthmatic Adults Only	6	441	Odds Ratio (M-H, Random, 95% CI)	0.58 [0.32, 1.07]
Asthmatic Children Only	6	409	Odds Ratio (M-H, Random, 95% CI)	0.40 [0.17, 0.94]

Comparison 7. PEFR

Outcome	No. of Studies	No. of Participants	Statistical method	Effect size
2 PEFR @ 60 min	6	132	Std. Mean Difference (IV, Random, 95% CI)	0.22 [-0.41, 0.86]
4 PEFR @ 120 min	1	56	Std. Mean Difference (IV, Random, 95% CI)	-0.36 [-0.89, 0.16]
5 Final PEFR	8	479	Mean Difference (IV, Random, 95% CI)	-7.91 [-15.98, 0.17]

Comparison 9. Symptoms scores

Outcome	No. of Studies	No. of Participants	Statistical method	Effect size

Controllers

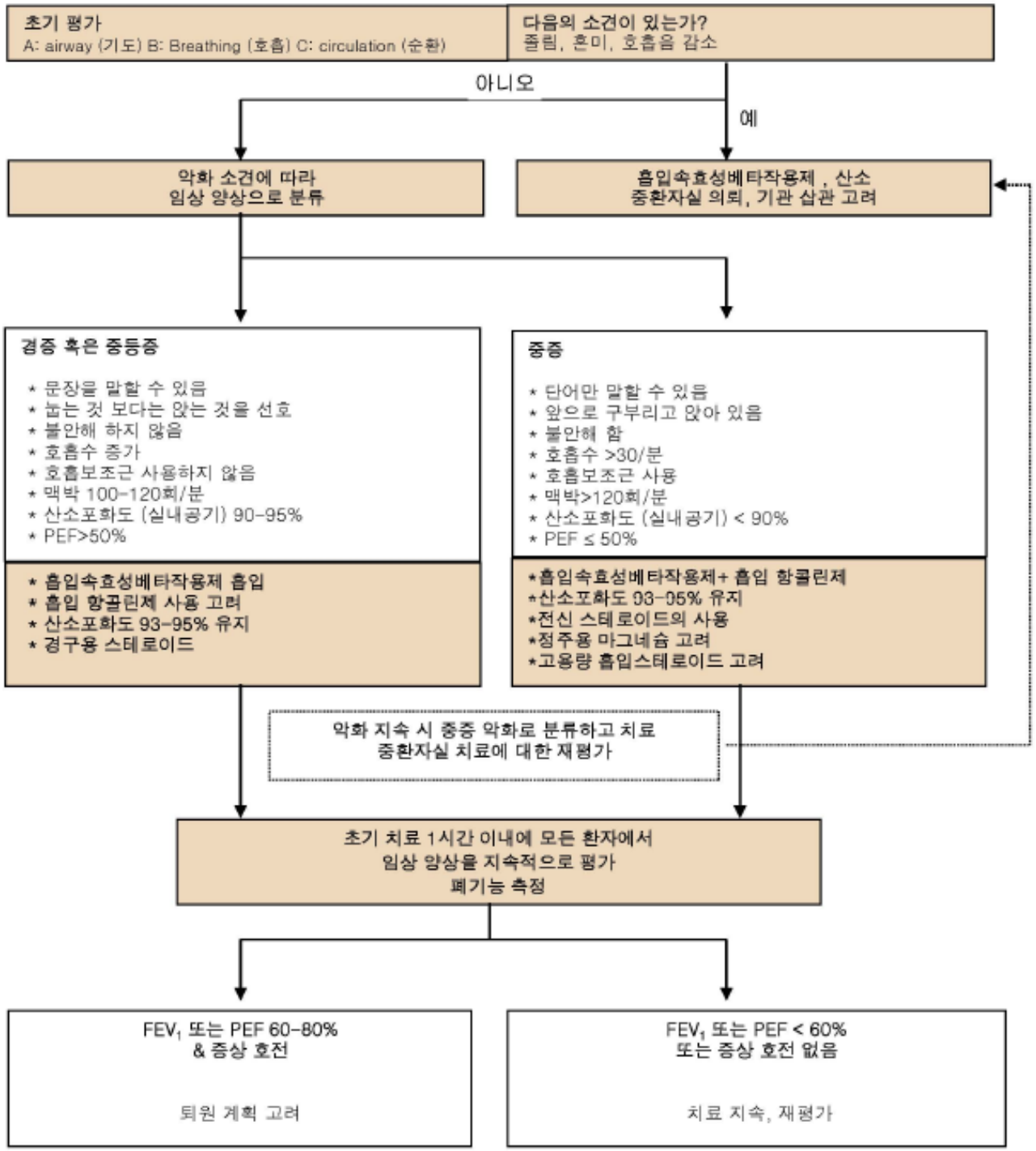
- Korean guideline
  - 흡입스테로이드(ICS)
    - 조절제로 저용량 ICS를 사용하는 환자는 2000 μg까지 증량
    - ICS를 이미 중간 용량 이상 사용하고 있는 경우에는 흡입스테로이드를 증량하기 보다는 경구스테로이드를 복용
    - 흡입스테로이드 투여를 하고 있지 않았던 환자에서는 흡입스테로이드의 투여를 시작
  - 천식 악화 시에는 추가적인 지속적인 집중 치료가 필요하다.

- GINA2014
  - Patients already prescribed controller medication should be provided with advice about increasing the dose for the next 2–4 weeks
  - ICS naïve patients → Regular ICS containing therapy

Medication	Short-term change (1-2 weeks) for worsening asthma	Evidence Level
Increase usual reliever:		
Short-acting beta$_2$-agonist (SABA)	Increase frequency of SABA use For pMDI, add spacer	A A
Low dose ICS/formoterol *	Increase frequency of reliever use (maximum formoterol total 72 mcg/day)	A
Increase usual controller:		
Maintenance and reliever ICS/formoterol *	Continue maintenance ICS/formoterol and increase reliever ICS/formoterol as needed* (maximum formoterol total 72 mcg/day)	A
Maintenance ICS with SABA as reliever	At least double ICS; consider increasing ICS to high dose (maximum 2000 mcg/day BDP equivalent)	B
Maintenance ICS/formoterol with SABA as reliever	Quadruple maintenance ICS/formoterol (maximum formoterol 72 mcg/day)	B
Maintenance ICS/salmeterol with SABA as reliever	Step up to higher dose formulation of ICS/salmeterol, or consider adding a separate ICS inhaler (to maximum total 2000 mcg/day BDP equivalent)	D
Add oral corticosteroids (OCS) and contact doctor		
OCS (prednisone or prednisolone)	Add OCS for severe exacerbations (e.g. PEF or FEV_1 <60% personal best or predicted), or patient not responding to treatment over 48 hours	A
	Adults: prednisolone 1 mg/kg/day (maximum 50 mg) usually for 5–7 days. *Children:* 1–2 mg/kg/day (maximum 40 mg) usually for 3–5 days.	D
	Tapering is not needed if OCS are prescribed for <2 weeks	B

병원에서의 치료 (ER)

- 산소
- SABA +/- SAMA
- (Epinephrine)
- 기타 기관지확장제
  - Ipratropium
  - theophylline
- 전신스테로이드
- 흡입스테로이드
- 마그네슘
- 항류코트리엔제
- NIV etc.



병원에서의 치료(ER)

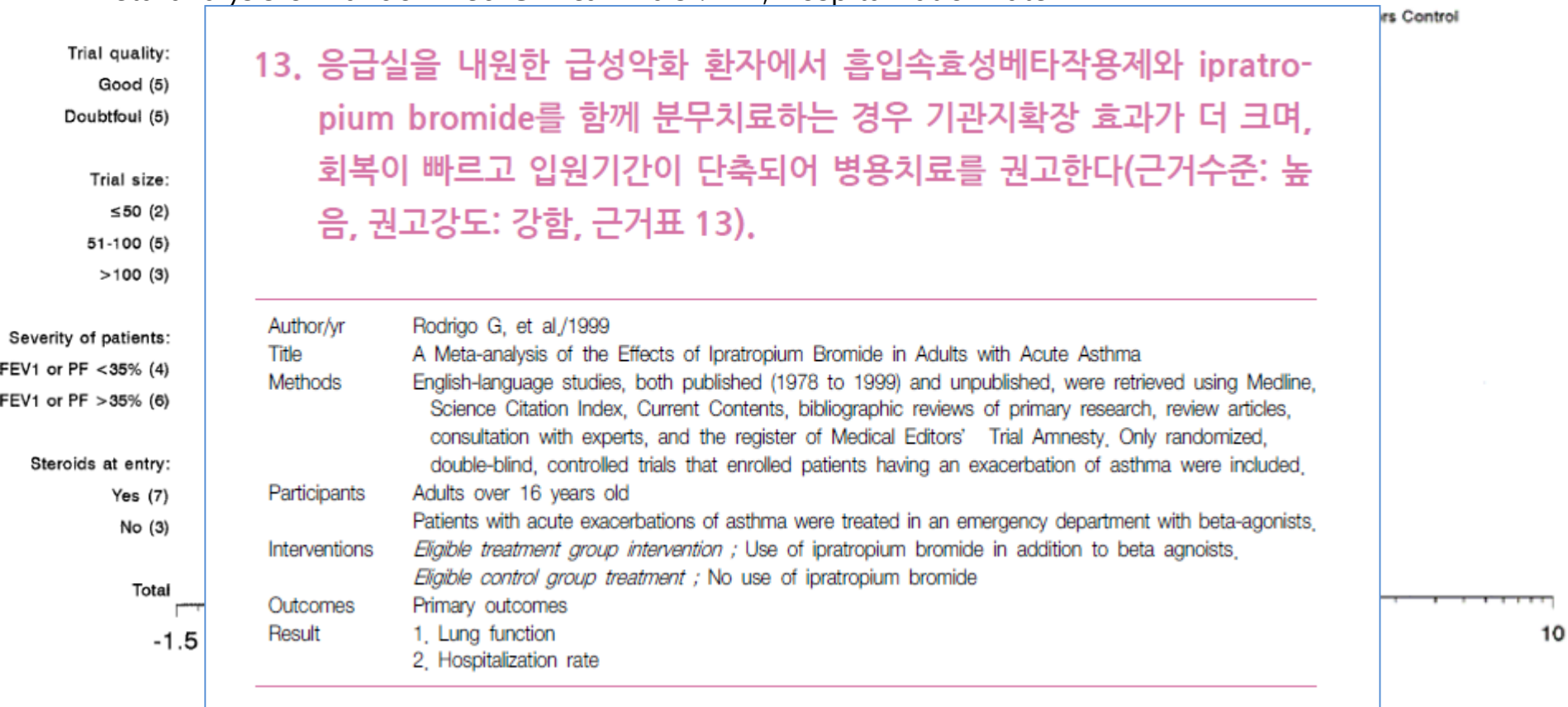
- Oxygen
  - Target arterial oxygen saturation 93~95%

- Bronchodilators
  - SABA with pMDI + spacer
    - 흡입속효성베타작용제는 급성악화의 치료 초기에는 지속적으로 흡입하다가 상태가 호전되면 필요할 때만 간헐적으로 흡입
  - Adding SAMA (Korean guideline)
    - 응급실을 내원한 급성악화 환자에서 SABA와 SAMA(ipratropium bromide)를 함께 분무 치료하는 경우 기관지확장 효과가 더 크며, 회복이 빠르고 입원기간이 단축되어 병용치료를 권고한다(근거수준: 높음, 권고강도: 강함, 근거표 13)
  - (S)MART (Korean guidline)
    - 지속성베타작용제인 formoterol은 비용 증가는 있으나 작용 시간이 속효성과 같이 빨리 나타나고 부작용은 증가하지 않아 흡입스테로이드(budesonide, beclomethasone)와 formoterol의 혼합제제를 급성 천식 악화의 조기에 증상 완화 효과를 위해 사용할수 있다
  - *cf. ICS/LABA combinations*
    - *The role of these medications in the emergency department or hospital is unclear*

Ipratropium in AEBA

Rodrigo G, et al./1999
A Meta-analysis of the Effects of Ipratropium Bromide in Adults with Acute Asthma : Lung function/Hospitalization

Stoodley RG, et al./1999
The Role of Ipratropium Bromide in the Emergency Management of Acute Asthma Exacerbation: A Meta-analysis of Randomized Clinical Trials : PEF, hospitalization rate



13. 응급실을 내원한 급성악화 환자에서 흡입속효성베타작용제와 ipratropium bromide를 함께 분무치료하는 경우 기관지확장 효과가 더 크며, 회복이 빠르고 입원기간이 단축되어 병용치료를 권고한다(근거수준: 높음, 권고강도: 강함, 근거표 13).

Author/yr	Rodrigo G, et al./1999
Title	A Meta-analysis of the Effects of Ipratropium Bromide in Adults with Acute Asthma
Methods	English-language studies, both published (1978 to 1999) and unpublished, were retrieved using Medline, Science Citation Index, Current Contents, bibliographic reviews of primary research, review articles, consultation with experts, and the register of Medical Editors' Trial Amnesty. Only randomized, double-blind, controlled trials that enrolled patients having an exacerbation of asthma were included.
Participants	Adults over 16 years old Patients with acute exacerbations of asthma were treated in an emergency department with beta-agonists.
Interventions	*Eligible treatment group intervention ;* Use of ipratropium bromide in addition to beta agnoists. *Eligible control group treatment ;* No use of ipratropium bromide
Outcomes	Primary outcomes
Result	1. Lung function 2. Hospitalization rate

Corticosteroids

- 전신스테로이드
  - 초기에 SABA를 흡입해도 효과가 불충분한 환자
  - 평소 경구스테로이드를 복용하던 환자에서 천식의 급성악화가 발생하였을 때
  - 이전 천식의 급성악화 시 전신스테로이드를 사용했던 환자
  - 용량: 하루 prednisolone으로 50 mg 1회 투여 혹은, hydrocortisone으로 200 mg/일 분할 주사
  - 기간: 5-7일

- 흡입스테로이드
  - 기관지확장효과: 흡입속효성베타작용제 단독 투여보다 흡입스테로이드제와의 병용투여
  - 재발 방지효과 :흡입스테로이드 =경구스테로이드
  - 고용량의 흡입스테로이드(하루 2.4 mg의 budesonide)는 하루 40 mg의 prednisolone과 비슷한 천식악화 예방효과

Magnesium

- IV magnesium
  - not recommended for routine use
  - a single 2 g infusion over 20 minutes
  - Reduces hospital admissions in some patients
    - adults with FEV1 <25–30% predicted at presentation
    - adults and children who fail to respond to initial treatment and have persistent hypoxemia
    - children whose FEV1 fails to reach 60% predicted after 1 hour of care (Evidence A)

- Inhaled magnesium
  - 흡입속효성베타작용제에 마그네슘 흡입치료를 추가하는 것은 입원율 감소 및 증상 개선에 도움이 되지 못하므로, 급성악화 환자에서 마그네슘 흡입치료를 하지 않을 것을 권고한다(근거수준: 낮음, 권고강도: 강함, 근거표 16)

  - Nebulized salbutamol is most often administered in normal saline; however, it can also be administered in isotonic magnesium sulfate.
  - While the overall efficacy of this practice is unclear, pooled data from three trials suggest possible improved pulmonary function in those with severe asthma exacerbations (FEV1 <50% predicted) (Evidence B)

16. 급성악화 환자에서 마그네슘 흡입치료를 하지 않을 것을 권고한다(근거 수준: 낮음, 권고강도: 강함, 근거표 16)

Goodacre 2013

Methods	Multicenter, double-blind, placebo controlled, three-arm, randomized trial

Bessmertny 2002

Methods

ospital
ation of Mg
trol: 358

es in 1 hour

aline

Outcomes

Gallegos-Solórzano 2010

Methods	RCT, parallel
Participants	Inclusion criteria: Adults, >18 years in the emergency dept with asthmatic crisis, FEV_1 < 60% predicted

Hughes 2003

Methods Design: parallel randomised controlled trial

Kokturk 2005

Methods	Parallel RCT
Participants	Inclusion criteria: moderate to severe asthma attacks, 18 to 60 years

Nannini 2000

Methods	Design: Randomised controlled trial. Method of randomisation: unknown. Concealment of allocation: yes. Blinding: double-blind, placebo-controlled. Solutions were pre-packaged in identical appearing vials. Withdrawals/dropouts: 3 patients were enrolled more than once, only the initial visit was used in the analysis

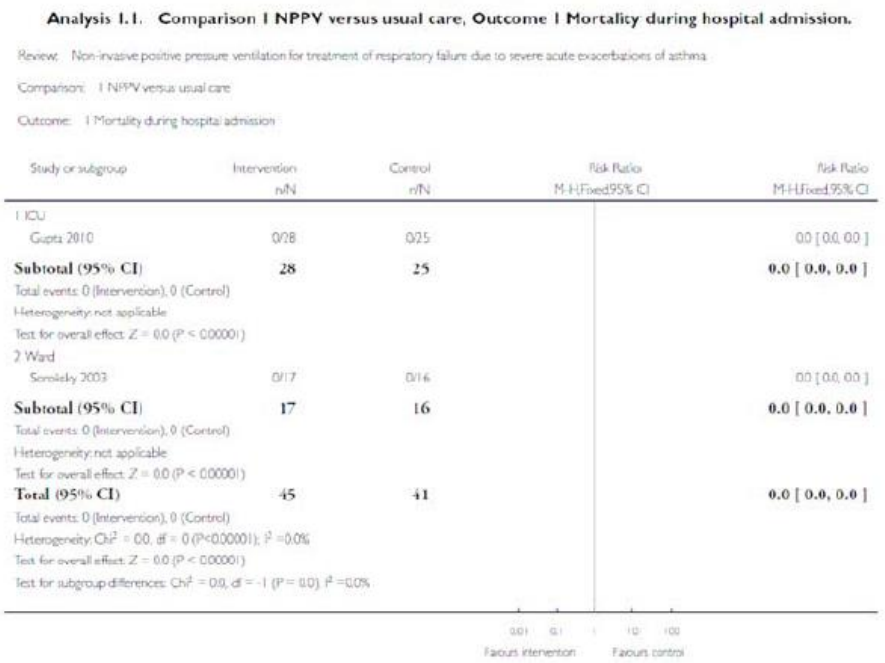
Notes

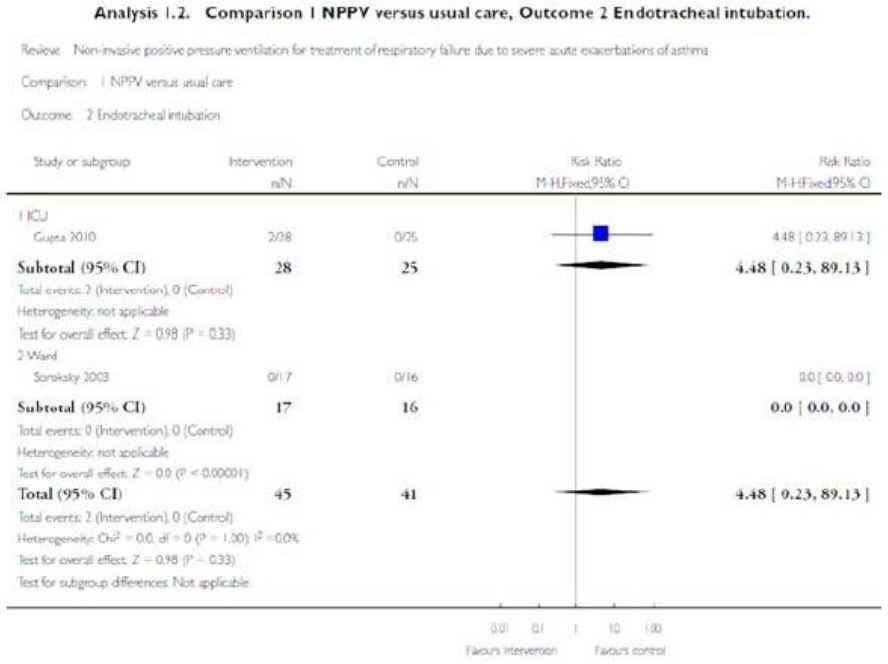
Risk of bias		
Bias	A	
Random sequence generation (selection bias)	L	
Allocation concealment (selection bias)	L	
Blinding of participants and personnel (performance bias)	Low risk	Double blind
Blinding of outcome assessment (detection bias)	Low risk	Double blind
Incomplete outcome data (attrition bias)	High risk	Follow up loss of assess
Selective reporting (reporting bias)	Low risk	Not apparent indication of selective reporting

NIV in AEBA

- GINA
  - The evidence regarding the role of NIV in asthma is weak.
  - Given the small size of the studies, no recommendation is offered.

- Korean guideline
  - 현재까지 중증 천식악화로 인한 호흡부전환자에서 비침습적 양압환기요법의 효과가 확립되지 않았으므로 적용여부를 신중하게 고려한다 (근거수준: 낮음, 권고강도: 약함, 근거표 17)





Antibiotics

- Korean guideline
  - Not commented

- GINA2014
  - Not recommended
  - Evidence does not support a role of antibiotics in asthma exacerbations unless there is strong evidence of lung infection (e.g. fever and purulent sputum or radiographic evidence of pneumonia). Aggressive treatment with corticosteroids should be implemented before antibiotics are considered.

Others

- Aminophyllines
- Helium oxygen therapy
- Leukotriene receptor antagonist
- Sedatives

응급실 퇴원 기준 및 입원 기준

- 입원
  - 내원 당시 폐기능이 자신의 최고치(혹은 예측치)의 25% 미만 또는 치료 후에도 40% 미만인 환자

- 퇴원
  - 치료 후 폐기능이 최고치나 예측치의 40~60% 정도이고 환자의 순응도가 좋고 적절한 진료가 가능한 경우
  - 치료 후 폐기능이 60% 이상

응급실 퇴원 시 고려 사항

- 경구스테로이드를 처방 (5-7일 이상)
- 기관지확장제는 필요에 따라 사용
- 흡입스테로이드 지속 사용
- 흡입기 사용 방법과 최대호기유량 측정기 사용법을 확인
- 급성악화 시 천식 행동지침
- 천식의 급성악화를 일으킨 원인을 규명하고 이를 피하도록 교육
- 퇴원 후 수일 내에 폐기능을 비롯한 기본적인 여러 변수가 정상화 될 때까지 주치의나 천식 전문의를 꾸준히 정기적으로 방문

Box 4-5. Discharge management after hospital or emergency department care for asthma

Medications

Oral corticosteroids (OCS)

Prescribe at least a 5–7 day course of OCS for adults (prednisolone or equivalent 1 mg/kg/day to a maximum of 50 mg/day) and 3–5 days for children (1–2 mg/kg/day to a maximum of 40 mg). For patients considered at risk of poor adherence, intramuscular corticosteroids may be considered[333] (Evidence B).

Reliever medication

Transfer patients back to as-needed rather than regular reliever medication use, based on symptomatic and objective improvement. If ipratropium bromide was used in the emergency department or hospital, it may be quickly discontinued, as it is unlikely to provide ongoing benefit.

Inhaled corticosteroids (ICS)

Initiate ICS prior to discharge, if not previously prescribed (Box 3-4, p30). Patients currently prescribed ICS-containing medication should generally have their treatment stepped up for 2–4 weeks (Box 4-2, p61) and should be reminded about the importance of adherence with daily use.

Risk factors that contributed to the exacerbation

Identify factors that may have contributed to the exacerbation and implement strategies to reduce modifiable risk factors (Box 3-8, p38). An exacerbation severe enough to require hospitalization may follow irritant or allergen exposure, inadequate long-term treatment, problems with adherence, and/or lack of a written asthma action plan, as well as unavoidable factors such as viral respiratory infections.

Self-management skills and written asthma action plan

- Review inhaler technique (Box 3-11, p42).
- Review technique with PEF meter if used.
- Provide a written asthma action plan (Box 4-2, p61) or review the patient's existing plan, either at discharge or as soon as possible afterwards. Patients discharged from the emergency department with an action plan and PEF meter have better outcomes than patients discharged without these resources.[362]
- Evaluate the patient's response to the exacerbation. If it was inadequate, review the action plan and provide written guidance to assist if asthma worsens again.[362,363]
- Review the patient's use of controller treatment before and during the exacerbation. Was it increased promptly and by how much? Were OCS added and if not, why not? Consider providing a short-course of OCS to be on hand for subsequent exacerbations.

Follow up appointment

A follow-up appointment within 2–7 days of discharge should be made with the patient's usual health care provider, to ensure that treatment is continued, that asthma symptoms are well controlled, and that the patient's lung function reaches their personal best (if known).

ICS: inhaled corticosteroids; OCS: oral corticosteroids; PEF: peak expiratory flow

요약

- 2014 국내 천식 지침 (급성 악화편)
  - GINA 2014 및 updated data를 바탕으로 문헌고찰을 통해서 천식의 급성악화 치료 시 고려되는 ICS, OCS, ipratropium bromide, inhaled magnesium, noninvasive ventilation의 유용성 여부에 대해서 권고 사항을 제시함.
  - User friendly?
  - Limitations
    - 약물 치료 이외의 급성 악화 관리 근거에 대한 고찰 필요
    - 의료 접근성의 차이가 있는 국내 현실을 반영한 action plan 또는 일차 의료 기관에서의 치료 및 교육 방향에 대한 추가 논의의 필요성

Q & A

THANKS FOR YOUR ATTENTION