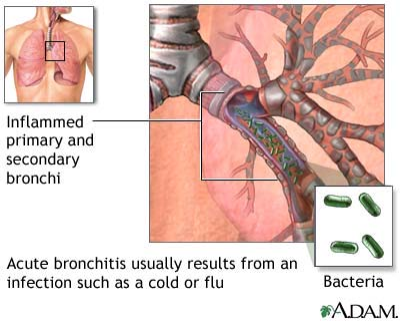
Médicaments et traitement de la bronchite (aiguë-chronique)

Françoise Van Bambeke

FARM2115

La bronchite aiguë: physiopathologie

- affection aiguë fréquente, d'origine **infectieuse**
- pathogènes respiratoires
  - → dommage de l'épithélium
    - → libération de cytokines
    - → inflammation
    - → sécrétions
    - → réduction de la motilité



Agents pathogènes: **virus**
rarement: *Mycoplasma pneumoniae*
Chlamydia pneumoniae
Bordetella pertussis

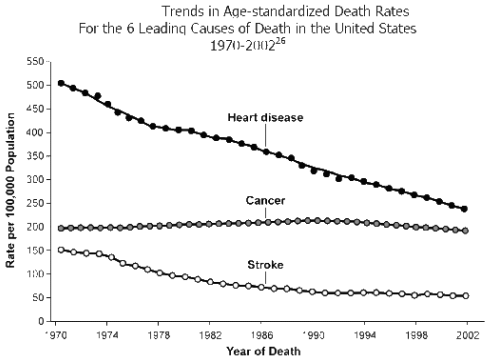
La bronchite chronique: physiopathologie

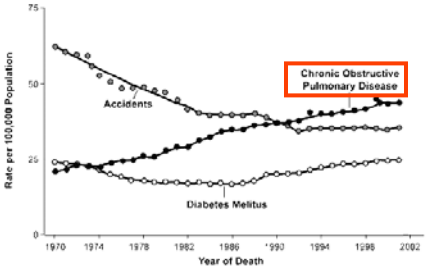
- Affection chronique **progressive** caractérisée par une limitation du flux d'air dans les bronches; partiellement réversible
- Origine : **réaction inflammatoire anormale** vis-à-vis de polluants aériens entraînant de la bronchoconstriction

cause majeure = fumée de cigarette
(50 % des fumeurs de plus de 50 ans !!)

Population à risque !

bronchite chronique et mortalité

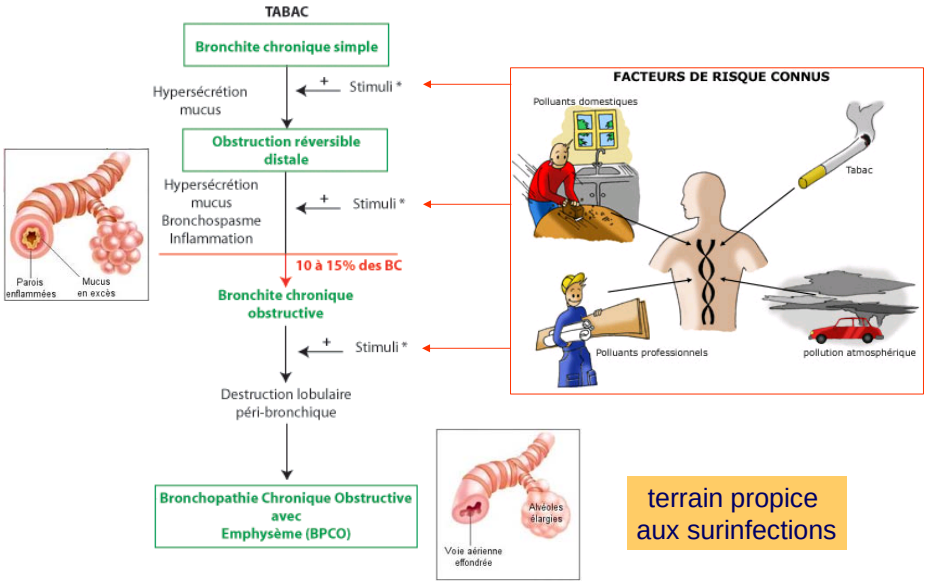




Reprinted from Jemal A, Ward E, Hao Y, Thun M. Trends in the leading causes of death in the United States, 1970-2002. JAMA 2005;294(10):1255S, with permission from JAMA

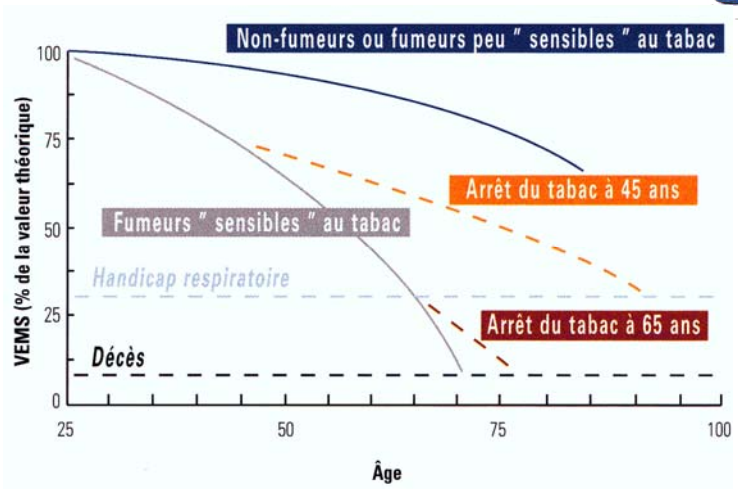
http://www.goldcopd.com

La bronchite chronique : physiopathologie



terrain propice aux surinfections

La bronchite chronique : tabac et fonction respiratoire



Bronchopathie chronique obstructive (BPCO) et exacerbations ….

- épisodes d'**aggravation de l'inflammation** et de la **dyspnée**
- favorisés par
  - des infections (souvent virales)
  - une exposition à des polluants
- accompagnés de **surinfections bactériennes** avec sécrétions purrulentes

Haemophilus influenzae
Moraxella catarrhalis
Neisseria spp
Streptococcus pneumoniae.
Chlamydia - Mycoplasma
Pseudomonas

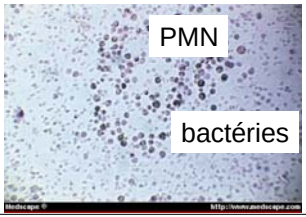
La bronchite aiguë et chronique: signes cliniques

Bronchite aiguë:

- toux aiguë, sans signe d'infection des voies supérieures, chez un patient sans antécédant d'affection pulmonaire.
- fièvre (peu)
- dyspnée et sifflements (parfois)
- chez l'enfant, laryngo-trachéo-bronchite
- (sputum)

Bronchite chronique:

- toux chronique, parfois non productive
- dyspnée progressive et persistante, aggravée par l'exercice
- sifflements
- sputum



La bronchite aiguë : traitement

Traitement symptomatique !

• Analgésique-antipyrétique à action anti-inflammatoire
  - aspirine (éviter chez l'enfant …)
  - ibuprofen

• Antitussifs

SI persistance > 6 jours : antibiotique
  • amoxicilline
  • macrolide (résistance !)

La bronchite chronique : traitement

Traitement non pharmacologique

• assainir l'environnement (polluants!)
• arrêter de fumer
• vacciner
  (grippe [réduction de mortalité de 50 %] -pneumonie)

Traitement pharmacologique

• Bronchodilatateurs:	agonistes β2 anticholinergiques (théophylline)	par inhalation
• Anti-inflammatoires	corticostéroïdes	
• (Fluidifiants des sécrétions	N-acétyl-cystéine)	

• Antibiotiques en cas d'exacerbation infectieuse

La bronchite chronique : traitement

Traitement non pharmacologique

- assainir l'environnement (polluants!)
- arrêter de fumer
- vacciner (grippe-pneumonie)

Strategy to Help a Patient Quit Smoking

1. **ASK**: Systematically identify all tobacco users at every visit.
   Implement an office-wide system that ensures that, for EVERY patient at EVERY clinic visit, tobacco-use status is queried and documented.
2. **ADVISE**: Strongly urge all tobacco users to quit.
   In a clear, strong, and personalized manner, urge every tobacco user to quit.
3. **ASSESS**: Determine willingness to make a quit attempt.
   Ask every tobacco user if he or she is willing to make a quit attempt at this time (e.g., within the next 30 days).
4. **ASSIST**: Aid the patient in quitting.
   Help the patient with a quit plan; provide practical counseling; provide intra-treatment social support; help the patient obtain extra-treatment social support; recommend use of approved pharmacotherapy if appropriate; provide supplementary materials.
5. **ARRANGE**: Schedule follow-up contact.
   Schedule follow-up contact, either in person or via telephone.

http://www.goldcopd.com

La bronchite chronique : traitement

Traitements pour le sevrage tabagique

Options thérapeutiques

Non-médicamenteuses

- prise en charge personnelle
- conseils par un médecin, un dentiste ou une infirmière
- soutien psychologique individuel, collectif ou par téléphone
- divers: thérapie d'aversion, exercices, acupuncture, hypnothérapie, thérapies comportementales, prévention de rechutes

Médicamenteuses

Traitement nicotinique

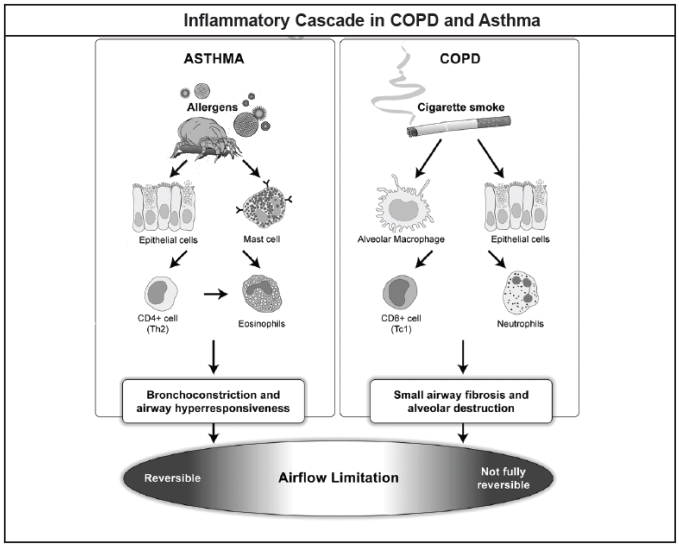
Médicaments de substitution sans nicotine

- bupropione
- nortriptyline*
- ISRS*
- anxiolytiques*
- clonidine*
- sélégiline*
- mécamylamine**
- naltrexone*
- cytisine**
- varénicline
- rimonabant*

* Le sevrage tabagique n'est pas une indication reprise dans la notice belge (juin 2008)
** Non disponible en Belgique (juin 2008)

CBIP, fiche de transparence 2008; mise à jour 2010

Asthme et bronchite chronique, un parallèle …



http://www.goldcopd.com

Médicaments bronchodilateurs

- β_2-mimétiques à courte durée d'action
  (action rapide; traitement de crise)
- β_2-mimétiques à longue durée d'action
  (traitement de fond)
- Antagonistes muscariniques:
  meilleur effet bronchodilatateur que dans l'asthme
  (tonus cholinergique)
  - ipratropium: antagoniste non spécifique; courte durée d'action
  - tiotropium: antagoniste spécifique M3; longue durée d'action

sous forme d'aérosol à poudre sèche :
peu adéquat chez les patients avec un faible capacité respiratoire !

Anticholinergiques

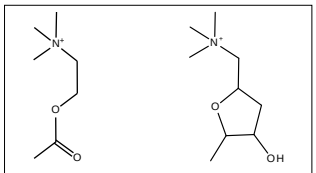
Le système cholinergique joue un rôle important dans la bronchopneumopathie obstructive chronique ... !!

- **ipratropium**: antagoniste non-spécifique (récepteurs M1, M2 et M3) et à courte durée d'action :
  - rarement utilisés seuls mais plutôt en association avec les β-2 agonistes (association fixes avec salbutamol/fénotérol)

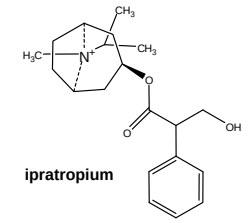
- **tiotropium**: antagoniste spécifique et à action prolongée
  → dissociation rapide du récepteur M2
  [récepteurs de rétrocontrôle; évite la libération réactionnelle d'acétylcholine]
  → dissociation lente des récepteurs M1 et M3
  [bronchodilatation prolongée]

  → indication uniquement dans le traitement de la BPCO

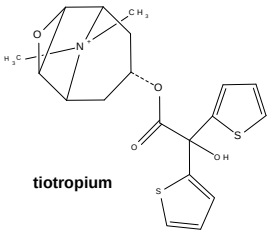
La spécialité ne fait l'objet d'un remboursement que lorsqu'elle est utilisée pour le traitement d'entretien de bénéficiaires atteints de bronchopneumopathies chroniques obstructives (BPCO), modérées à très sévères (stade II, III et IV de la nouvelle classification GOLD 2003, pour "Global Initiative for Chronic Obstructive Lung Disease, updated 2003").



acétylcholine muscarine

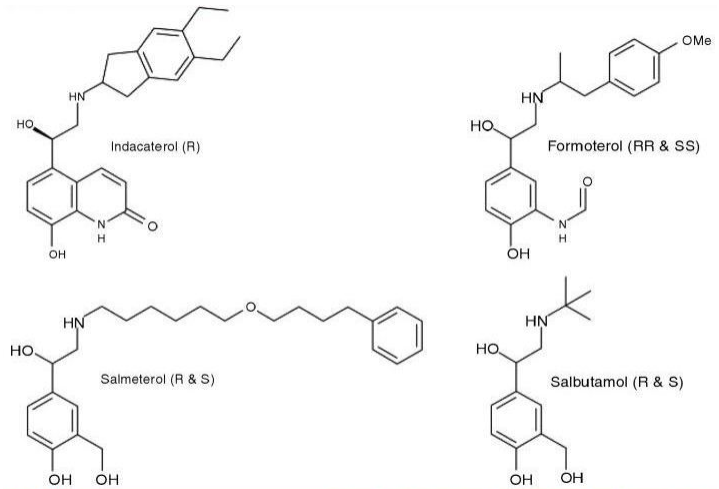


ipratropium



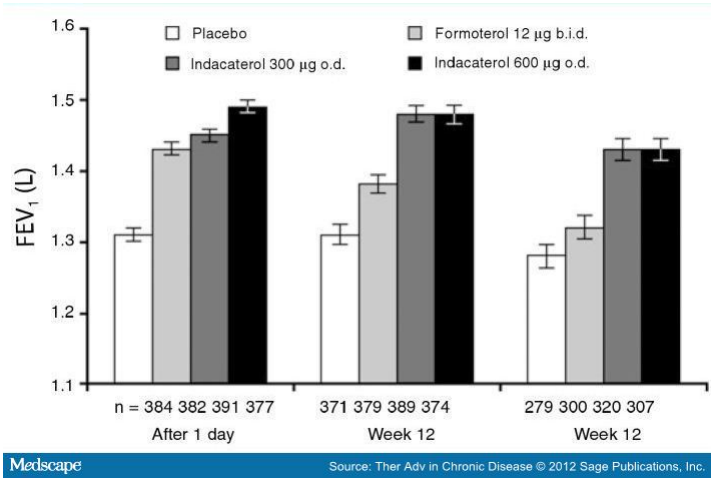
tiotropium

Indacatérol: β_2 mimétique à LDA pour la BPCO



Indacatérol: β_2 mimétique à LDA pour la BPCO

+ efficace à long terme; 1 dose par jour !



Ther Adv Chronic Dis. 2012;3(1):25-36, Thorax 2010;65:473-479.

Beta-bloquants et pathologies respiratoires

Folia Pharmacotherapeutica Article. Février 2012

Bêta-bloquants chez les patients atteints de BPCO ou d'asthme

Abstract

- Chez les *patients atteints de BPCO* , la plupart des auteurs s'accordent à dire que les β-bloquants cardiosélectifs peuvent être utilisés de manière sûre lorsqu'un β-bloquant est indiqué pour l'une ou l'autre raison (par ex. après un infarctus du myocarde). Lors de l'administration de la première dose, il convient toutefois d'observer le patient vu la possibilité d'apparition d'un bronchospasme. En ce qui concerne les β-bloquants non cardiosélectifs, les données sont plus limitées.
- Chez les *patients asthmatiques* , il convient d' être encore plus prudent en ce qui concerne l'utilisation de ces médicaments.

Chez les patients asthmatiques ou atteints de BPCO traités par un β-bloquant (le plus souvent un β-bloquant non cardiosélectif), des bronchospasmes aigus sont décrits. C'est pourquoi les β-bloquants, surtout les β-bloquants non cardiosélectifs, sont classiquement contre-indiqués chez les patients asthmatiques ou atteints de BPCO. Ces dernières années, des nuances ont été apportées à ces contre-indications.

BPCO

Comme le mentionne le Répertoire Commenté des Médicaments, il est généralement admis que la BPCO constitue une contre-indication relative à l'utilisation de β-bloquants. Il y a cependant de plus en plus de preuves attestant que les β-bloquants cardiosélectifs (à savoir avec une sélectivité β_1 : acébutolol, aténolol, bétaxolol, bisoprolol, céliprolol, esmolol, métoprolol, nébivolol) peuvent être utilisés de manière sûre chez les patients atteints de BPCO.

La plupart des auteurs s'accordent à dire que les β-bloquants cardiosélectifs peuvent être utilisés chez des patients atteints de BPCO lorsqu'un β-bloquant est indiqué pour l'une ou l'autre raison (par ex. après un infarctus du myocarde). Lors de l'administration de la première dose, il convient toutefois d'observer le patient vu la possibilité d'apparition d'un bronchospasme. Si un bronchospasme devait survenir, les auteurs de l'éditorial dans le British Medical Journal sont d'avis qu'il est préférable d' administrer un anticholinergique par inhalation [n.d.l.r.: le traitement par le β-bloquant peut en principe être poursuivi].

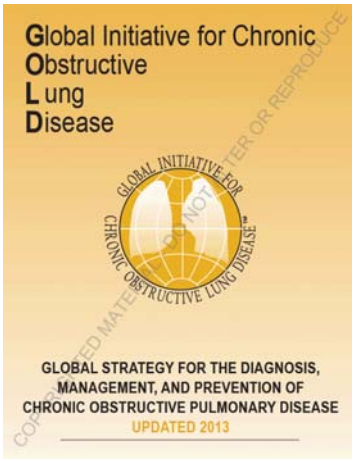
Les données en ce qui concerne l'utilisation de β-bloquants non cardiosélectifs chez les patients atteints de BPCO sont plus limitées. Vu leurs propriétés pharmacologiques, une plus grande prudence est de rigueur.

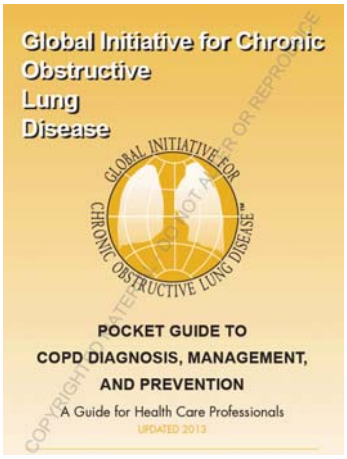
Asthme

Dans le Répertoire, l'asthme figure comme contre-indication pour les β-bloquants, surtout, mais pas exclusivement, pour les β-bloquants non cardiosélectifs. Une analyse d'études randomisées réalisée par la *Cochrane Collaboration* a evalué l'usage de β-bloquants cardiosélectifs en cas d'asthme. Il en ressort que, chez les patients présentant un asthme léger à modérément sévère, l'administration d'une dose unique d'un β-bloquant cardiosélectif diminue légèrement le VEMS, sans toutefois augmenter les symptômes respiratoires ou diminuer la réponse aux β_2 -mimétiques. Dans des études d'une durée de 3 à 28 jours, aucune diminution du VEMS ou de la réponse aux β_2 -mimétiques n'a été observée; il est même suggéré que les β-bloquants cardiosélectifs sans activité sympathomimétique intrinsèque (tels que le métoprolol, le bisoprolol) augmentent la réponse aux β_2 -mimétiques. On ne dispose pas de données en ce qui concerne les patients atteints d'un asthme grave, ou l'utilisation prolongée de β-bloquants et de leurs conséquences éventuelles sur la fréquence ou la gravité des exacerbations aiguës d'asthme. [*Cochrane Database Syst Rev* 2002; 4Art. No.:CD002992 (contenu mis à jour jusqu'au 03/06/07; doi:10.1002/14651858.CD002992); ; *Lancet* 2009; 373: 104-5]

Ces résultats nuancent quelque peu la notion de contre-indication des β-bloquants cardiosélectifs dans l'asthme léger à modérément sévère.

Algorithme de traitement de la BPCO recommandations GOLD





http://www.goldcopd.com

Evaluation de la capacité respiratoire

indice de Tiffeneau : FEV1 /FVC ratio (*VEMS/CVF)*

Volume expiré en 1 sec / capacité expiratoire maximale
(Valeur normale ~ 80 %)

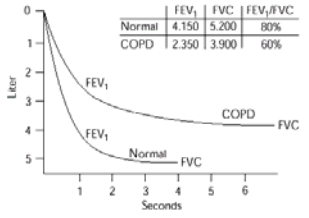


Figure 1. Normal spirogram and spirogram typical of patients with mild to moderate chronic obstructive pulmonary disease. Calculation of FEV_1, FVC, and FEV_1/FVC ratio is also shown. Reprinted from Management of COPD, component 1: Assess and monitor disease. In: Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO workshop report. Global Initiative for Chronic Obstructive Lung Disease. Available at http://www.goldcopd.com/workshop/ch5p1.html. Accessed 5 September 2001.

Table 3. Classification of Severity of Airflow Limitation in COPD (Based on Post-Bronchodilator FEV_1)

In patients with $FEV_1/FVC < 0.70$:		
GOLD 1:	Mild	$FEV_1 \geq 80\%$ predicted
GOLD 2:	Moderate	$50\% \leq FEV_1 < 80\%$ predicted
GOLD 3:	Severe	$30\% \leq FEV_1 < 50\%$ predicted
GOLD 4:	Very Severe	$FEV_1 < 30\%$ predicted

http://www.goldcopd.com

Evaluation de la capacité respiratoire

Sévérité de l'altération de la fonction respiratoire sur base d'un questionnaire

Table 2.4. Modified Medical Research Council Questionnaire for Assessing the Severity of Breathlessness

PLEASE TICK IN THE BOX THAT APPLIES TO YOU (ONE BOX ONLY)

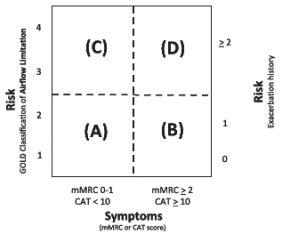
mMRC Grade 0. I only get breathless with strenuous exercise.	☐
mMRC Grade 1. I get short of breath when hurrying on the level or walking up a slight hill.	☐
mMRC Grade 2. I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level.	☐
mMRC Grade 3. I stop for breath after walking about 100 meters or after a few minutes on the level.	☐
mMRC Grade 4. I am too breathless to leave the house or I am breathless when dressing or undressing.	☐

http://www.goldcopd.com

Algorithme de traitement - GOLD

Table 4. Combined Assessment of COPD

*When assessing risk, choose the **highest risk** according to GOLD grade or exacerbation history. (One or more hospitalizations for COPD exacerbations should be considered high risk.)*



Patient	Characteristic	Spirometric Classification	Exacerbations per year	mMRC	CAT
A	Low Risk Less Symptoms	GOLD 1-2	≤ 1	0-1	< 10
B	Low Risk More Symptoms	GOLD 1-2	≤ 1	≥ 2	≥ 10
C	High Risk Less Symptoms	GOLD 3-4	≥ 2	0-1	< 10
D	High Risk More Symptoms	GOLD 3-4	≥ 2	≥ 2	≥ 10

mMRC: Modified British Medical Counsil Breathlessness test

http://www.goldcopd.com

Algorithme de traitement - GOLD

Table 6. Non-Pharmacologic Management of COPD

Patient Group	Essential	Recommended	Depending on Local Guidelines
A	Smoking cessation (can include pharmacologic treatment)	Physical activity	Flu vaccination Pneumococcal vaccination
B, C, D	Smoking cessation (can include pharmacologic treatment) Pulmonary rehabilitation	Physical activity	Flu vaccination Pneumococcal vaccination

mMRC: Modified British Medical Counsil Breathlessness test

http://www.goldcopd.com

Algorithme de traitement - GOLD

Table 7: Pharmacologic Therapy for Stable COPD*

Patient Group	RECOMMENDED FIRST CHOICE	ALTERNATIVE CHOICE	OTHER POSSIBLE TREATMENTS**
A	SA anticholinergic prn *or* SA $beta_2$-agonist prn	LA anticholinergic *or* LA $beta_2$-agonist *or* SA $beta_2$-agonist and SA anticholinergic	Theophylline
B	LA anticholinergic *or* LA $beta_2$-agonist	LA anticholinergic and LA $beta_2$-agonist	SA $beta_2$-agonist *and/or* SA anticholinergic Theophylline
C	ICS + LA $beta_2$-agonist *or* LA anticholinergic	LA anticholinergic and LA $beta_2$-agonist *or* LA anticholinergic and PDE-4 Inhibitor *or* LA $beta_2$-agonist and PDE-4 Inhibitor	SA $beta_2$-agonist *and/or* SA anticholinergic Theophylline
D	ICS + LA $beta_2$-agonist *and/or* LA anticholinergic	ICS + LA $beta_2$-agonist and LA anticholinergic *or* ICS + LA $beta_2$-agonist and PDE-4 inhibitor *or* LA anticholinergic and LA $beta_2$-agonist *or* LA anticholinergic and PDE-4 inhibitor	Carbocysteine SA $beta_2$-agonist *and/or* SA anticholinergic Theophylline

**Medications in each box are mentioned in alphabetical order and therefore not necessarily in order of preference.*

***Medications in this column can be used alone or in combination with other options in the First and Alternative Choice columns*

Glossary:
SA: short-acting
LA: long-acting
ICS: inhaled corticosteroid
PDE-4: phosphodiesterase-4
prn: when necessary

http://www.goldcopd.com

Place des médicaments - GOLD

bronchodilatateurs

Table 3.4. Bronchodilators in Stable COPD

- Bronchodilator medications are central to symptom management in COPD.
- Inhaled therapy is preferred.
- The choice between beta$_2$-agonist, anticholinergic, theophylline, or combination therapy depends on availability and individual patient response in terms of symptom relief and side effects.
- Bronchodilators are prescribed on an as-needed or on a regular basis to prevent or reduce symptoms.
- Long-acting inhaled bronchodilators are convenient and more effective at producing maintained symptom relief than short-acting bronchodilators.
- Combining bronchodilators of different pharmacological classes may improve efficacy and decrease the risk of side effects compared to increasing the dose of a single bronchodilator.

http://www.goldcopd.com

Place des médicaments - GOLD

bronchodilatateurs

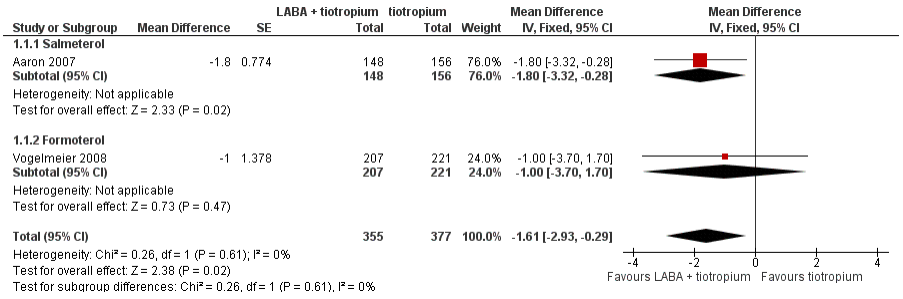
Combination bronchodilator therapy. Although monotherapy with long-acting β_2-agonists appears to be safe[411,412], combining bronchodilators with different mechanisms and durations of action may increase the degree of bronchodilation for equivalent or lesser side effects[440]. For example, a combination of a short-acting β_2-agonist and an anticholinergic produces greater and more sustained improvements in FEV_1 than either drug alone and does not produce evidence of tachyphylaxis over 90 days of treatment[126,147,148] (**Evidence A**). In a large study, combination therapy that includes a long-acting inhaled bronchodilator/anti-inflammatory combination (salmeterol/fluticasone propionate) compared to the long-acting bronchodilator (tiotropium) showed no difference in exacerbation rate although more patients randomized to combination treatment completed the study[425].

http://www.goldcopd.com

Place des médicaments - GOLD

bronchodilatateurs

LABA + tiotropium / tiotopium ~ quality of life



Mais pas de différence sur la mortalité ou les exacerbations ….

Karner & Cates, Cochrane Database Syst Rev. 2012 Apr 18;4

Place des médicaments - GOLD

corticoïdes

Inhaled Corticosteroids. The dose-response relationships and long-term safety of inhaled corticosteroids in COPD are not known. Only moderate to high doses have been used in long-term clinical trials. The efficacy and side effects of inhaled corticosteroids in asthma are dependent on the dose and type of corticosteroid[239], but whether this is also the case in COPD is unclear. The effects of corticosteroids on pulmonary and systemic inflammation in patients with COPD are controversial, and their role in the management of stable COPD is limited to specific indications.

Regular treatment with inhaled corticosteroids improves symptoms, lung function, and quality of life, and reduces the frequency of exacerbations[144] in COPD patients with an FEV_1 < 60% predicted[195,240-244] (**Evidence A**). Withdrawal from treatment with inhaled corticosteroids may lead to exacerbations in some patients[245]. Regular treatment with inhaled corticosteroids does not modify the long-term decline of FEV_1 nor mortality in patients with COPD[126,175,176,195,246,247,520] (**Evidence A**).

http://www.goldcopd.com

Place des médicaments - GOLD

corticoïdes

Combination Inhaled Corticosteroid/Bronchodilator Therapy. An inhaled corticosteroid combined with a long-acting beta$_2$-agonist is more effective than the individual components in improving lung function and health status and reducing exacerbations in patients with moderate (**Evidence B**) to very severe COPD[195,240,243,244,246,251-253,521,522] (**Evidence A**). A large prospective clinical trial failed to demonstrate a statistically significant effect of combination therapy on mortality[195], but a subsequent meta-analysis found that combination therapy may reduce mortality with a number needed to treat (NNT) of 36[254] (**Evidence B**). Combination therapy is associated with an increased risk of pneumonia[255], but no other significant side effect (**Evidence A**). The addition of a long-acting beta$_2$-agonist/ inhaled corticosteroid combination to tiotropium improves lung function and quality of life[256,257] and may further reduce exacerbations (**Evidence B**) but more studies of triple therapy are needed[258].

http://www.goldcopd.com

Place des médicaments - GOLD

mucolytiques

Mucolytic (mucokinetic, mucoregulator) agents (ambroxol, erdosteine, carbocysteine, iodinated glycerol). The regular use of mucolytics in COPD has been evaluated in a number of long-term studies with controversial results[187-189]. Although a few patients with viscous sputum may benefit from mucolytics[190,191], the overall benefits seem to be very small, and the widespread use of these agents cannot be recommended at present (**Evidence D**). There is some evidence, however, that in COPD patients who have not been treated with inhaled glucocorticosteroids, treatment with mucolytics such as carbocisteine may reduce exacerbations[426].

xanthines

. Theophylline is effective in COPD, but due to its potential toxicity inhaled bronchodilators are preferred when available. All studies that have shown efficacy of theophylline in COPD were done with slow-release preparations.

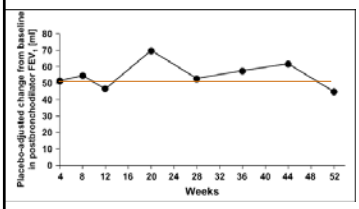
http://www.goldcopd.com

un médicament pour demain ?

roflumilast

Approuvé pour la BPCO
- par l'EMEA en avril 2010
- par la FDA en mars 2011

Phosphodiesterase-4 inhibitors. The principal action of phosphodiesterase-4 inhibitors (PDE4-inhibitors) is to reduce inflammation through inhibition of the breakdown of intracellular cyclic AMP. The PDE4-inhibitor, roflumilast, has been approved for use only in some countries. It is a once daily oral medication with no direct bronchodilator activity, although it has been shown to improve FEV_1 in patients treated with salmeterol or tiotropium[454].



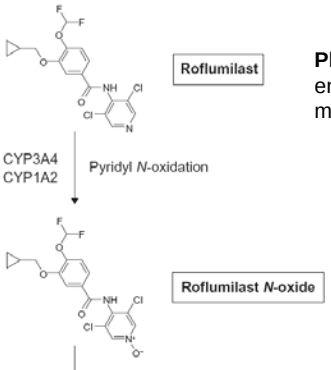
→ indiqué au grade IV

ANALYSIS OF EXACERBATIONS

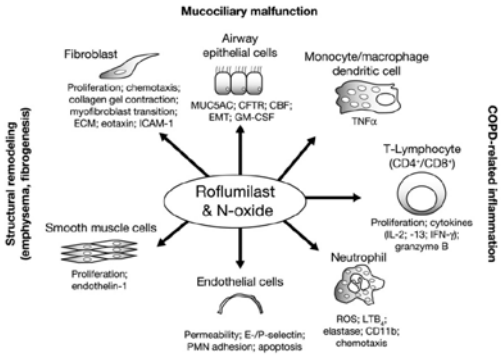
Exacerbations	Rate/Patient/yr* Roflumilast (*n* = 760)	Rate/Patient/yr* Placebo (*n* = 753)	Effect Size* Rate Ratio (*SE*)	Effect Size* Difference versus Placebo (%)	p Value†
Overall moderate or severe exacerbations	0.857	0.918	0.934 (0.075)	6.6	0.451
Moderate exacerbations requiring systemic corticosteroids	0.395	0.483	0.816 (0.090)	18.4	0.029
Moderate or severe exacerbations requiring systemic corticosteroids	0.474	0.549	0.864 (0.090)	13.6	0.183
Moderate or severe exacerbations in patients in GOLD stage IV	1.014	1.588	0.639 (0.131)	36.1	0.024

http://www.goldcopd.com; Am J Respir Crit Care Med. 2007 176:154-61

un médicament pour demain ?



Phosphodiesterase 4 (PDE4)
enzyme métabolisant AMPc dans les cellules inflammatoires, musculaires lisses des bronches, nerveuses pulmonaires



Drug Des Devel Ther. 2010 4:147-58; Pulm Pharmacol Ther. 2010 23:235-56

un médicament pour demain ?

Mais … faible rapport bénéfice-risque !

	Roflumilast (%) (*n* = 4459)	Placebo (%) (*n* = 4239)	RR (95% CI)	Risk difference (95% CI)	NNH (95% CI)
All AEs	2096 (47)	1172 (28)	1.11 (1.03 to 1.19)	0.19 (0.17 to 0.21)	5 (5 to 6)
Gastrointestinal	715 (16)	181 (4.7)	4.50 (3.13 to 6.47)	0.12 (0.11 to 0.13)	8 (8 to 9)
Musculoskeletal	70 (1.6)	49 (1.2)	1.44 (1.00 to 2.07)	0.004 (–0.001 to 0.009)	241 (–1283 to 110)
Infectious	740 (17)	751 (18)	0.98 (0.84 to 1.15)	-0.011 (–0.027 to 0.005)	–90 (–37 to 216)
Nervous system	189 (4.2)	79 (1.9)	2.43 (1.88 to 3.15)	0.024 (0.017 to 0.031)	42 (32 to 60)
Psychiatric	53 (1.2)	22 (0.5)	2.43 (1.48 to 3.98)	0.007 (0.003 to 0.011)	149 (93 to 351)
Weight loss	329 (7.4)	90 (2.1)	4.22 (2.70 to 6.60)	0.05 (0.04 to 0.06)	19 (16 to 23)
AE leading to discontinuation	669 (15)	392 (9.2)	1.63 (1.45 to 1.84)	0.06 (0.04 to 0.07)	17 (14 to 23)

AE, adverse event; CI, confidence interval; NNH, number needed to harm; RR, relative risk.

→ A l'heure actuelle, commercialisé dans quelques pays seulement (Allemagne, UK, Danemark)

Oba and Lone, Ther Adv Respir Dis. 2012 Nov 29. [Epub ahead of print]

Exacerbation: prise en charge globale

1. Vérifier la technique d'inhalation
2. Bronchodilatateurs (association)
3. Augmenter la dose/fréquence de bronchodilatateurs
4. Améliorer la forme d'administration (chambre d'expansion)
5. Corticoïdes oraux si pas d'amélioration dans les deux jours et si pas de contre-indication

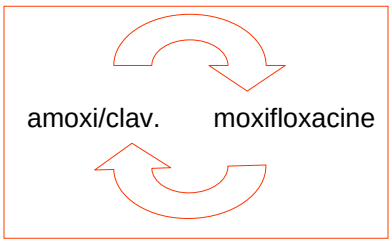
- Pas de place pour les mucolytiques
- Pas de place pour la théophilline

Exacerbation: traitement antibiotique

SI surinfection : antibiotique

- premier choix: beta-lactame (amoxi / (clav) ou cephalo II
- alternative si allergie IgE médiée: moxifloxacine

- si > 3 exacerbations/ an : alternance



si comorbidités / sputum purulent

(Klebsiella, *Pseudom.*, Gram (-))

fluoroquinolone (ciprofloxacine [MAIS dose !!])

éventuellement cephalosporine III, amoxi/clav, carbapenème

Importance de la technique d'inhalation !

Table 5 Percentage of observations of inhaler technique (yes = at least a critical error; no = no inhaler error) for the groups of asthmatic and COPD subjects according to some unscheduled health-care resources use in the last year.

Characteristic	COPD			Asthma			OR ± SE; P level[a,b]
At least a critical inhaler error	No		Yes	No		Yes	
Hospital admissions, %							
Never	62	>	55	86	>	76	1.47 ± 0.17; $p = 0.001$
1	23	<	26	9	<	13	
2–3	11	<	16	3	<	9	
>3	4	<	3	2	<	2	
Emergency department visits, %							
Never	71	>	64	81	>	69	1.62 ± 0.20; $p = 0.0006$
1	22	<	24	11	>	16	
2–3	4	<	10	3	<	10	
>3	3	<	2	4	<	5	
Antimicrobic courses, %							
Never	30	>	20	41	>	34	1.50 ± 0.15; $p = 0.00004$
1	29	<	31	30	>	25	
2–3	26	<	33	18	=	17	
>3	15	<	15	11	<	14	
Corticosteroid courses, %							
Never	37	>	29	35	>	27	1.54 ± 0.16; $p = 0.00003$
1	22	>	19	30	>	35	
2–3	30	>	26	22	>	19	
>3	11	<	26	13	<	19	

[a] Relationship between risk of at least a critical inhaler error and self-report of some unscheduled health-care resources use in the last year.
[b] Ordered logistic regression adjusted by diagnosis and type of inhaler and evaluated by $\chi 2$

Melani et al, Respir Med. 2011;105:930-8

Une étude belge en officine ouverte au public

COPD Management in Primary Care: An Observational, Community Pharmacy–Based Study

Els Mehuys, Koen Boussery, Els Adriaens, Luc Van Bortel, Leen De Bolle, Inge Van Tongelen, Jean-Paul Remon, and Guy Brusselle

The Annals of Pharmacotherapy ▪ *2010 February, Volume 44*

BACKGROUND: Chronic obstructive pulmonary disease (COPD) is a prevalent disease that is frequently treated in primary care. However, data regarding the primary care management of COPD are scarce. Such observational data are necessary to detect problem areas and to develop targeted interventions for improvement of COPD management.

OBJECTIVE: To provide a detailed description of (1) drug therapy, (2) drug adherence, (3) inhalation technique, and (4) health status of patients with COPD recruited via community pharmacies.

METHODS: A cross-sectional, observational study was conducted in 93 pharmacies in Belgium. Participants (N = 555) completed a questionnaire collecting information on personal characteristics, smoking history, influenza vaccination, COPD medication, and adverse effects. Adherence to COPD maintenance medication was analyzed 1 year retrospectively through prescription refill rates. Inhalation technique was scored using a checklist. Health status was evaluated with the St. George's Respiratory Questionnaire, the Clinical COPD Questionnaire, and the Modified Medical Research Council dyspnea scale.

RESULTS: The mean age of the patients was 68.6 years; 73.7% were men and 37.2% were current smokers. The influenza vaccination status was significantly lower in patients aged less than 65 years (65.7%) than in patients aged 65 years or more (86.2%) ($p < 0.001$). Fixed combinations of inhaled corticosteroids and long-acting β_2-agonists were the most frequently used COPD medications (75.4%). About 48% of patients were underadherent (<80% adherence), 47% were adherent (80–120% adherence) and 5% were overadherent (>120% adherence). Predictors for underadherence were age and number of drugs. Twenty-one percent of patients made major inhalation technique errors with rescue medication; these were all errors in handling pressurized metered-dose inhalers (pMDIs).

CONCLUSIONS: This observational study on COPD management in primary care highlights 4 main aspects that could be improved: (1) drug adherence, (2) inhalation technique with pMDIs, (3) influenza vaccination in COPD patients younger than 65 years, and (4) smoking cessation.

Une étude belge en officine ouverte au public

Table 1. Patient Characteristics[a]

Parameter	N = 555
Male sex	409 (73.7)
Age, y	68.6 ± 9.6
50–60	117 (21.1)
61–70	189 (34.1)
71–80	185 (33.3)
≥80	64 (11.5)
BMI, kg/m²	26.0 ± 4.8
<21[b]	77 (13.9)
≥21	478 (86.1)
Education	
no high school degree	361 (65.0)
high school degree	119 (21.4)
academic degree	75 (13.5)
Smoking status	
current smoker	207 (37.3)
ex-smoker	336 (60.5)
never smoked[c]	12 (2.2)
passive smoker	82 (14.8)[d]
Pack-years of current smokers	35.3 ± 20.7
Pack-years of ex-smokers	46.4 ± 30.6
COPD duration, y	11 ± 14.2
Influenza vaccination	436 (78.6)
COPD management supervised by	
GP only	218 (39.3)
pneumologist only	38 (6.8)
both GP and pneumologist	299 (53.9)

BMI = body mass index; COPD = chronic obstructive lung disease.
[a]Data are presented as mean ± SD or n (%).
[b]BMI values lower than 21 are associated with an increased risk of death.[23]
[c]The treating physician was contacted to confirm the diagnosis of COPD.
[d]Percentage calculated on the total study population (ie, 82/555).

Table 2. Drug Therapy[a]

COPD medication	
SABA	13.1
LABA	11.7
short-acting anticholinergics ± SABA	41.0
long-acting anticholinergics	58.9
ICS	14.5
ICS + LABA combination	75.4
theophylline	15.4
leukotriene modifiers	4.1
oral corticosteroids	6.1
Number of COPD medications, median (range)	2 (1–6)
≥1 adverse event of COPD medication	25.3
Inhalation technique controller medication	
% of correct steps, median	85.7
pts. scoring 100%	31.9
pts. scoring 0%	3.5
Inhalation technique rescue medication	
% of correct steps, median	85.7
pts. scoring 100%	27.3
pts. scoring 0%	21.0
Adherence to controller medication[b]	
adherence rate, median[c]	81.1
pts. with adherence rate <80%	48.2
pts. with adherence rate 80–120%	46.8
pts. with adherence rate >120%	4.9

COPD = chronic obstructive pulmonary disease; ICS = inhaled corticosteroids; LABA = long-acting β-agonists; SABA = short-acting β-agonists.
[a]Data are presented as %, unless otherwise stated.
[b]Calculated for 491 patients (64 patients had incomplete pharmacy records).
[c]Expressed as %, which is the ratio of dispensed medication to prescribed medication.

Plus d'info ?

- Global Initiative for COPD (GOLD)
  http://www.goldcopd.com
- Fiche de transparence sur le sevrage tabagique
  http://www.cbip.be/pdf/tft/TF_Taba.pdf
- Documentation INAMI
  http://www.inami.fgov.be/drug/fr/drugs/groups/asthma_bpco_copd/pdf/prospectus.pdf
- Recommandations BAPCOC traitement antibiotique
  http://www.health.belgium.be/eportal/Myhealth/Care/Properuse/Antibiotics/Humanmedicine/Recommendations/index.htm