COPD: acetylcysteïne 6506

FEV_1: forced expiratory volume in 1 second, FEF25-75: force midexpiratory volume.

CONCLUSIE
Er is geen onderbouwing voor een contra-indicatie. De verschillende studies geven aan dat acetylcysteïne juist een positief effect zou kunnen hebben bij COPD-patiënten.

PICO

P(atient)	Patiënten met COPD
I(ntervention)	Gebruik van acetylcysteïne
C(omparison / Control)	Patiënten zonder COPD
O(utcome)	Risico op (verergering) luchtwegklachten

Datum literatuursearch: 03-01-2017

PUBMED

Zoekterm: acetylcysteine AND copd

Bron	Bewijs	Resultaten/Opmerkingen
ref. 1 Cazzola M et al. Influence of N-acetylcysteine on chronic bronchitis or COPD exacerbations: a meta-analysis. Eur Respir Rev 2015;24:451-61.	meta-analyse n=1933 (aantal patiënten met COPD dat acetylcysteïne gebruikt)	In order to clarify the possible role of N-acetylcysteine (NAC) in the treatment of patients with chronic bronchitis and chronic obstructive pulmonary disease (COPD), we have carried out a meta-analysis testing the available evidence that NAC treatment may be effective in preventing exacerbations of chronic bronchitis or COPD and evaluating whether there is a substantial difference between the responses induced by low (≤ 600 mg per day) and high (> 600 mg per day) doses of NAC. The results of the present meta-analysis (13 studies, 4155 COPD patients, NAC n = 1933; placebo or controls n = 2222) showed that patients treated with NAC had significantly and consistently fewer exacerbations of chronic bronchitis or COPD (relative risk 0.75, 95% CI 0.66-0.84; p < 0.01), although this protective effect was more apparent in patients without evidence of airway obstruction. However, high doses of NAC were also effective in patients suffering from COPD diagnosed using spirometric criteria (relative risk 0.75, 95% CI 0.68-0.82; p = 0.04). NAC was well tolerated and the risk of adverse reactions was not dose-dependent (low doses relative risk 0.93, 95% CI 0.89-0.97; p = 0.40; high doses relative risk 1.11, 95% CI 0.89-1.39; p = 0.58). The strong signal that comes from this meta-analysis leads us to state that if a patient suffering from chronic bronchitis presents a documented airway obstruction, NAC should be administered at a dose of ≥ 1200 mg per day to prevent exacerbations, while if a patient suffers

ref. 1, vervolg		from chronic bronchitis, but is without airway obstruction, a regular treatment of 600 mg per day seems to be sufficient.
ref. 2 Erdil N et al. The effects of N-acetylcysteine on pulmonary functions in patients undergoing on-pump coronary artery surgery: a double blind placebo controlled study. Eur Rev Med Pharmacol Sci 2016;20:180-7.	studie (prospectief, dubbelblind, placebogecontroleerd) n=10 (aantal patiënten met COPD dat acetylcysteïne krijgt)	Interventie: acetylcysteïne 600 mg 3 dagen, n=10. Controle: placebo, n=20. Populatie: COPD patiënten die coronaire chirurgie ondergaan met cardiopulmonale bypass. Resultaten: - FEV_1 is postoperatief 4,55% afgenomen in de placebogroep - FEF25-75 is postoperatief 4,2% afgenomen in de placebogroep - FEV_1 en FEF25-75 zijn in de interventiegroep niet significant afgenomen Opmerking auteurs: het aantal patiënten met COPD was relatief klein
ref. 3 Tse HN et al. Benefits of high-dose N-acetylcysteine to exacerbation-prone patients with COPD. Chest 2014;146:611-23.	studie (dubbelblind, gerandomiseerd en placebogecontroleerd) n=58 (aantal patiënten met COPD dat acetylcysteïne krijgt)	BACKGROUND: Although high-dose N-acetylcysteine (NAC) has been suggested to reduce COPD exacerbations, it is unclear which category of patients with COPD would benefit most from NAC treatment. The objective of this study was to compare the effect of high-dose NAC (600 mg bid) between high-risk and low-risk Chinese patients with COPD. METHODS: Patients with spirometry-confirmed stable COPD were randomized to treatment with either NAC 600 mg bid or placebo in addition to their usual treatments. Patients were followed up every 16 weeks for a total of 1 year. Further analysis was performed according to each patient's exacerbation risk at baseline as defined by the current GOLD (Global Initiative for Chronic Obstructive Lung Disease) strategy to analyze the effect of high-dose NAC in high-risk and low-risk patients. RESULTS: Of the 120 patients with COPD randomized (men, 93.2%; mean age, 70.8 ± 0.74 years; prebronchodilator FEV_1, 53.9 ± 2.0%; baseline characteristics comparable between treatment groups), 108 (NAC, 52; placebo, 56) completed the 1-year study. For high-risk patients (n = 89), high-dose NAC compared with placebo significantly reduced exacerbation frequency (0.85 vs 1.59 [P = .019] and 1.08 vs 2.22 [P = .04] at 8 and 12 months, respectively), prolonged time to first exacerbation (P = .02), and increased the probability of being exacerbation free at 1 year (51.3% vs 24.4%, P = .013). This beneficial effect of high-dose NAC vs placebo was not significant in low-risk patients. CONCLUSIONS: High-dose NAC (600 mg bid) for 1 year reduces exacerbations and prolongs time to first exacerbation in high-risk but not in low-risk Chinese patients with COPD.
ref. 4 Zheng JP et al. Twice daily N-acetylcysteine 600 mg for exacerbations of chronic obstructive	studie (prospectief, gerandomiseerd, dubbelblind, placebogecontroleerd)	BACKGROUND: Increased oxidative stress and inflammation has a role in the pathogenesis of chronic obstructive pulmonary disease (COPD). Drugs with antioxidant and anti-inflammatory properties, such as N-acetylcysteine, might

pulmonary disease (PANTHEON): a randomised, double-blind placebo-controlled trial. Lancet Respir Med 2014;2:187-94.	n=504 (aantal patiënten met COPD dat acetylcysteïne gebruikt)	provide a useful therapeutic approach for COPD. We aimed to assess whether N-acetylcysteine could reduce the rate of exacerbations in patients with COPD. METHODS: In our prospective, randomised, double-blind, placebo-controlled, parallel-group study, we enrolled patients aged 40-80 years with moderate-to-severe COPD (post-bronchodilator forced expiratory volume in 1 s [FEV1]/forced vital capacity <0·7 and FEV1 of 30-70% of predicted) at 34 hospitals in China. We stratified patients according to use of inhaled corticosteroids (regular use or not) at baseline and randomly allocated them to receive N-acetylcysteine (one 600 mg tablet, twice daily) or matched placebo for 1 year. The primary endpoint was the annual exacerbation rate in patients who received at least one dose of study drug and had at least one assessment visit after randomisation. This study is registered with the Chinese Clinical Trials Registry, ChiCTR-TRC-09000460. FINDINGS: Between June 25, 2009, and Dec 29, 2010, we screened 1297 patients, of whom 1006 were eligible for randomisation (504 to N-acetylcysteine and 502 to placebo). After 1 year, we noted 497 acute exacerbations in 482 patients in the N-acetylcysteine group who received at least one dose and had at least one assessment visit (1·16 exacerbations per patient-year) and 641 acute exacerbations in 482 patients in the placebo group (1·49 exacerbations per patient-year; risk ratio 0·78, 95% CI 0·67-0·90; p=0·0011). N-acetylcysteine was well tolerated: 146 (29%) of 495 patients who received at least one dose of N-acetylcysteine had adverse events (48 serious), as did 130 (26%) of 495 patients who received at least one dose of placebo (46 serious). The most common serious adverse event was acute exacerbation of COPD, occurring in 32 (6%) of 495 patients in the N-acetylcysteine group and 36 (7%) of 495 patients in the placebo group. INTERPRETATION: Our findings show that in Chinese patients with moderate-to-severe COPD, long-term use of N-acetylcysteine 600 mg twice daily can prevent exacerbations, especially in disease of moderate severity. Future studies are needed to explore efficacy in patients with mild COPD (GOLD I). FUNDING: Hainan Zambon Pharmaceutical.

OVERIGE

Bron	**Effect**
ref. 5 SPC Fluimucil (conc. voor infusieopl.) 12-09-11	Bw: Overgevoeligheidsreacties, zoals ernstige ademnood met bronchospasme zijn bij intraveneus gebruik van acetylcysteïne als antidotum voor paracetamolintoxicaties gerapporteerd.

ref. 6 SPC Fluimucil (vernevelvlst.) 28-07-14*	Bw: soms: overgevoeligheid (omvat o.a. bronchospasmen, dyspneu en angio-oedeem)

* SPC Acetylcysteïne Teva (oraal poeder) 01-02-16 bevat dezelfde informatie.

RISICOFACTOREN

Risicofactoren	-

	Contra-indicatie	**Actie**	**Datum**
Beslissing deskundigen	Nee	Nee	11 mei 2017