Astma: acetylcysteïne 1421

CONCLUSIE
In de SPC's wordt gewaarschuwd om astmapatiënten extra te monitoren gedurende de therapie. Ook worden bijwerkingen als bronchospasmen genoemd. De literatuur is niet volledig eenduidig. De meerderheid van de studies vindt echter geen relatie tussen toediening van acetylcysteïne en verergering van astma of optreden van bronchospasmen.

PICO

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

Datum literatuursearch: 23-12-2016

PUBMED

Zoekterm: acetylcysteine AND asthma

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 from chronic bronchitis, but is without airway obstruction, a regular treatment of 600 mg per day seems to be sufficient.
ref. 2 Carlsten C et al. Anti-oxicant N-acetylcysteine diminishes diesel exhaust-induced increased airway responsiveness in person with airway hyper-reactivity. Toxicol Sci 2014;139:479-87.	studie (gerandomiseerd, dubbelblind, cross-over) n = 16 (aantal patiënten met astma dat acetylcysteïne gebruikt)	BACKGROUND: Inhalation of diesel exhaust (DE) at moderate concentrations causes increased airway responsiveness in asthmatics and increased airway resistance in both healthy and asthmatic subjects, but the effect of baseline airway responsiveness and anti-oxidant supplementation on this dynamic is unknown. OBJECTIVES: We aimed to determine if changes in airway responsiveness due to DE are attenuated by thiol anti-oxidant supplementation, particularly in those with underlying airway hyper-responsiveness. METHODS: Participants took N-acetylcysteine (600 mg) or placebo capsules three times daily for 6 days. On the last of these 6 days, participants were exposed for 2 h to either filtered air (FA) or DE (300 μg/m(3) of particulate matter smaller than 2.5 microns). Twenty-six non-smokers were studied under each of three experimental conditions (filtered air with placebo, diesel exhaust with placebo, and diesel exhaust with N-acetylcysteine) using a randomized, double-blind, crossover design, with a 2-week washout between conditions. Methacholine challenge was performed pre-exposure (baseline airway responsiveness) and post-exposure (effect of exposure). RESULTS: Anti-oxidant supplementation reduced baseline airway responsiveness in hyper-responsive individuals by 20% (p = 0.001). In hyper-responsive individuals, airway responsiveness increased 42% following DE compared with FA (p = 0.03) and this increase was abrogated with anti-oxidant supplementation (diesel exhaust with N-acetylcysteine vs. filtered air with placebo, p = 0.85). CONCLUSIONS: Anti-oxidant (N-acetylcysteine) supplementation protects against increased airway responsiveness associated with DE

		inhalation and reduces need for supplement bronchodilators in those with baseline airway hyper-responsiveness. Individuals with variants in genes of oxidative stress metabolism when exposed to DE are protected from increases in airway responsiveness if taking anti-oxidant supplementation.
ref. 3 Yamamoto T et al. Incidence and management of N-acetylcysteine-related anaphylactoid reactions during the management of acute paracetamol overdose. Eur J Emerg Med 2014;21:57-60.	studie (retrospectief) n = 12 (aantal patiënten met astma dat acetylcysteïne gebruikt)	OBJECTIVE: Adverse drug reactions (ADRs) to N-acetylcysteine (NAC) treatment for paracetamol overdose are typically anaphylactoid in origin and occur in 2-48% of treated patients. We explored the incidence and management of NAC ADR in our unit. PATIENTS AND METHODS: Case notes of patients who presented with paracetamol overdose and had ADR to NAC between February 2005 and June 2011 were reviewed. A total of 1648 patients presented with suspected paracetamol overdose and 660 received NAC treatment. Within this group, 82 patients had documented NAC-related ADR. RESULTS: Asthma and female sex, which are reported risk factors for ADR, did not lead to the development of more severe ADR (P=0.771 and 0.330, respectively). CONCLUSION: The incidence of ADR to NAC was comparable with published studies, although there was no association of severity with asthma or female sex. The management of ADRs is variable, with frequent, inappropriate use of steroids. Education about the pathophysiology of these ADRs may improve management.
ref 4. Schmidt LE. Identification of patients at risk of anapylactoid reactions to N-acetylcysteine in the treatment of paracetamol overdose. Clin Toxicol (Phila) 2013;51:467-72.	studie (retrospectief) n=77 (aantal patiënten met astma dat acetylcysteïne gebruikt)	• 19 astmapatiënten hadden bijwerkingen (8,4% van totaal aantal patiënten met bijwerkingen) • 58 astmapatiënten zonder bijwerkingen (5,9% van totaal aantal patiënten zonder bijwerkingen) geen significant verschil
ref. 5 Schmidt LE et al. Risk factors in the development of adverse reactions to N-acetylcysteine in patients with paracetamol poisoning.	studie (retrospectief) n = 33 (aantal patiënten met astma dat acetylcysteïne gebruikt)	Patiënten met paracetamolintoxicatie worden behandeld met acetylcysteïne (i.v. infuus, 15 min: 150 mg/kg, 4 uur: 50 mg/kg, 16 uur: 100 mg/kg). 33 patiënten hebben astma. 5 patiënten ontwikkelen bronchospasmen, waarvan 1 met astma. Astmapatiënten hebben een 4,3 maal groter risico op systemische bijwerkingen (o.a. bronchospasmen, angio-oedeem) dan

Br J Clin Pharmacol 2001;51:87-91.		patiënten zonder astma, maar de bijwerkingen verschillen niet in intensiteit.

OVERIGE

Bron	Effect
ref. 6 SPC Fluimucil (conc. voor infusieopl.) 12-09-11	Waarschuwing*:* Patiënten die leiden aan astma bronchiale dienen nauwgezet te worden gevolgd gedurende de therapie, aangezien bronchospasmen kunnen optreden. Wanneer er zich een bronchospasme voordoet, dienen adequate maatregelen genomen te worden. Bw: Overgevoeligheidsreacties, zoals ernstige ademnood met bronchospasme zijn bij intraveneus gebruik van acetylcysteïne als antidotum voor paracetamolintoxicaties gerapporteerd.
ref. 7 SPC Fluimucil (vernevelvlst.) 28-07-14	Waarschuwing: Patiënten die leiden aan astma bronchiale dienen nauwgezet te worden gevolgd gedurende de therapie, aangezien bronchospasmen kunnen optreden. Wanneer er zich een bronchospasme voordoet, dient de behandeling onmiddellijk te worden gestaakt. Bw: soms: overgevoeligheid (omvat o.a. bronchospasmen, dyspneu en angio-oedeem)
ref. 8 SPC Acetylcysteïne Teva (oraal poeder) 01-02-16	Waarschuwing: Bij patiënten die leiden aan astma bronchiale kunnen bronchospasmen optreden. Wanneer er zich een bronchospasme voordoet, dient het gebruik onmiddellijk te worden gestaakt. Bw: soms: overgevoeligheid (omvat o.a. bronchospasmen, dyspneu en angio-oedeem)

RISICOFACTOREN

Risicofactoren	-

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