Astma: opioïden 0071

CONCLUSIE
Er is geen onderbouwing voor een contra-indicatie.
Werkgroep KNMP 28-04-2004: voorzichtigheid is geboden bij COPD, bij astma zijn geen problemen te verwachten.

PICO

P(atient)	patiënten met astma
I(ntervention)	opioïdgebruik
C(omparison / Control)	placebo
O(utcome)	risico op (verergering) luchtwegklachten

Datum literatuursearch: 31-05-2017

PUBMED
Zoekterm: "Asthma"[MeSH] AND Humans[Mesh] AND (english[Language] OR dutch[Language]) AND ("Analgesics, Opioid"[Mesh] OR opioid OR morphine OR alfentanil OR buprenorphine OR codeine OR dextromoramide OR diamorphine OR fentanyl OR hydromorphone OR methadone OR nalbuphine OR nicomorphine OR oxycodone OR pentazocine OR pethidine OR piritramide OR remifentanil OR sufentanil OR tapentadol OR tramadol)

Bron	Bewijs	Resultaten/Opmerkingen
ref. 1 McNicol et al. Management of opioid side effects in cancer-related and chronic noncancer pain: a systematic review. Journal of Pain 2003;4:231-56.	review	Opioïden werken op het ademhalingscentrum en kunnen een dosisafhankelijke ademhalingsdepressie veroorzaken. Therapeutische dosering kan de ademhalingsfrequentie en -diepte verminderen. Meestal leidt een compensatiemechanisme tot handhaving van normale arteriële zuurstofconcentraties. Tolerantie voor bijwerkingen van opioïden treedt meestal binnen enkele dagen tot weken op waardoor ademhalingsdepressie bij langdurig gebruik zelden voorkomt. Oraal gebruik en geleidelijke dosisverhoging vermindert daardoor het risico hierop.
ref. 2 Yamanaka T, et al. Opioid effect on lungs. Respirology 2013; 18: 255-62.	review	Retrospective data of patients admitted with asthma exacerbations also suggests a link with the use of opioids. Multiple small case series have demonstrated that patients using heroin, by nasal insufflations for the majority, but also smoking or intravenous injection, are more frequently admitted with asthma exacerbations. A retrospective case control study by Krantz et al. of 84 patients admitted to the ICU for asthma exacerbations showed positive urine drug screen for opioids in 65% of those who were screened, nearly double the overall rate. Levine observed that of 152 patients admitted to an ICU for asthma exacerbations in Chicago, 17% of heroin users were intubated versus 2.3% of other patients. A review of patients in a drug treatment facility showed an overall asthma rate of approximately 5% in drug users and when further analyzed, 97% of the asthmatic patients were opioid users. Furthermore, 28%

		described a temporal relationship between asthma symptoms and heroin use. These studies suggest that asthma exacerbation is significantly worsened by the use or abuse of opioids. Some studies suggest that opioids do not have any effect on airway resistance. A small study of asthma patients compared naloxone versus placebo pretreatment followed by methacholine. Compared to placebo, naloxone-treated patients showed a significant increase in respiratory rate, dyspnoea and a drop in inspiratory time. However, there was no significant change in FEV1 compared to placebo.
ref. 3 Burburan SM, et al. Anaesthetic management in asthma. Minerva Anestesiol 2007; 73: 357-65.	review	OPIOIDS Although opioids could release histamine, they are considered safe for patients with increased bronchial reactivity. Fentanyl and its analogues are frequently used in the induction of anaesthesia, and they can lead to thorax rigidity that can be misinterpreted as bronchospasm. With slow injection, this effect is hardly observed. Moreover, the suppression of the cough reflex and the deepening of anaesthesia level achieved after opioid administration can be helpful in asthmatic patients.
ref. 4 Otulana B, et al. Safety and pharmacokinetics if inhaled morphine delivered using the AERx system in patients with moderate-to-severe asthma. Int J Clin Pharmacol Ther 2004; 42: 456-62	studie (enkelblind crossover) n=20 (n=aantal patiënten met astma en morfine per inhalatie)	OBJECTIVE: The safety and pharmacokinetics of inhaled morphine in asthmatic subjects were investigated using the AERx System, a novel aerosol system. METHODS: Twenty subjects with asthma received inhaled placebo and inhaled morphine sulfate, 2.2 mg, 4.4 mg and 8.8 mg, on separate days in a single-blind crossover study. Six of the subjects received an additional open-label dose of 17.6 mg on a separate day. Plasma morphine concentrations and safety evaluations including pulmonary function testing were performed. RESULTS: Mean tmax values were similar following all dose groups at approximately 1-2 minutes. Mean AUC(0-->1) values showed dose proportionality for the first 3 dose groups (6.3, 12.3 and 24.3 ng x h x ml(-1)), the mean AUC(0-->1) for the 17.6 mg dose group was 1.6x that of the 8.8 mg dose group. No statistically significant differences in forced expiratory volume in 1 sec (FEV1) were found for the 2.2 mg, 4.4 mg, or 8.8 mg dose groups; at 17.6 mg, a statistically significant but not clinically meaningful reduction in mean FEV1 (-8.18%) from baseline occurred at 10 minutes compared to placebo, spontaneously returning to baseline by 60 min. Four subjects experienced significant but reversible decreases in FEV1 of > or = 20% compared to baseline and across all dose levels including after placebo, but with no associated increase in dyspnea, wheezing or other adverse events. CONCLUSIONS: Inhaled morphine using the AERx System was absorbed rapidly and demonstrated dose-dependent plasma concentrations. It was well-tolerated and did not cause clinically significant bronchoconstriction in most subjects with moderate-to-severe asthma.
ref. 5 Groeben H. Strategies in the patient with compromised respiratory function. Best Pract Res Clin Anaesthesiol 2004; 18: 579-94.	review	Today opioids are one of the main components of general anaesthesia. When alfentanil or sufentanil are used on induction of anaesthesia, thorax rigidity can be observed and easily misinterpreted as bronchospasm. This effect increases with increasing speed of injection and with the age of the patient.57 With slow injection, it is hardly observed at all. Otherwise, despite histamine release on injection of very high doses of morphine, opioids are unproblematic drugs in patients with increased bronchial reactivity. Sometimes the suppression of cough and the deepening of anaesthesia can be used beneficially in patients with obstructive airway disease.

ref. 6 Bellofiore S, et al. Endogenous opioids modulate the increase in ventilatory output and dyspnea during severe acute bronchocontriction. Am. Rev. Respir. Dis. 1990; 142: 812–16.		The aim of this study was to evaluate whether endogenous opioids are involved in the regulation of breathing pattern and respiratory drive during bronchoconstriction induced by methacholine (MCh). We studied six male asymptomatic asthmatics 18 to 35 yr of age. In a preliminary study we determined the concentration of MCh causing a 60% fall in FEV1 (PC60 FEV1). On two subsequent days, we measured breathing pattern, dyspnea sensation (Borg scale), mouth occlusion pressure (P0.1), and FEV1 before and 10 min after an intravenous injection of either naloxone (0.1 mg/kg) or saline according to a randomized double-blind crossover design. A MCh concentration equal to the PC60 FEV1 was then inhaled, and measurements were repeated 5 min later. Neither placebo nor naloxone affected baseline breathing pattern, P0.1, and FEV1. Naloxone pretreatment did not influence airway response to MCh; the mean percent fall in FEV1 was 65.9 +/- 1.3 and 64.7 +/- 1.2% (mean +/- 1 SE) on the placebo day and the naloxone day, respectively. After MCh inhalation no significant changes in VE, VT, and breathing frequency occurred when patients received placebo. However, P0.1 increased from 1.48 +/- 0.17 to 3.43 +/- 0.70 cm H2O (p less than 0.05), and VT/TI fell from 0.66 +/- 0.08 to 0.52 +/- 0.04 L/s (p less than 0.05). Naloxone pretreatment resulted in an increase in breathing frequency (from 18.2 +/- 1.7 to 22.8 +/- 2.6 breaths/min; p less than 0.05) and VT/TI (from 0.58 +/- 0.06 to 0.74 +/- 0.05 L/s; p less than 0.05) after MCh.(ABSTRACT TRUNCATED AT 250 WORDS)

OVERIGE

Bron	**Effect**
ref. 7 SPC Rapifen (alfentanil) 09-12-16 e.a. *[1]	CI: slechte longfunctie i.v.m. ademhalingsdepressieve werking. Waarschuwing: ademhalingsdepressie die dosis gerelateerd is. (Een significante ademhalingsdepressie zal optreden bij toediening van een dosis boven 1 mg alfentanil, 200 µg fentanyl). Bw: vaak: apneu, ademhalingsdepressie (waaronder met fataal gevolg); soms: bronchospasme, hoesten, (terugkeren van) ademhalingsdepressie; zeer zelden: ademhalingsstilstand.
ref. 8 SPC Temgesic (buprenorfine) 15-03-2016	CI: ernstige respiratoire insufficiëntie, asthma bronchiale. Waarschuwing: veroorzaakt net als andere werkende dempende analgetica respiratoire depressie, daarom is voorzichtigheid geboden bij patiënten met ademhalingstoornissen. Bw: vaak: hypoventilatie; soms: dyspneu; zelden: apneu. Tijdens het gebruik van buprenorfine als substitutiebehandeling werd eveneens respiratoire depressie waargenomen. Gevallen van bronchospasme werden eveneens gemeld.
ref. 9 SPC Codeinefosfaat Ratiopharm 02-03-16 e.a.*[2]	CI: verminderde ademhalingsreserve (astma bronchiale, emfyseem). Bw: ademhalingsdepressie.
ref. 10 SPC Tramal (tramadol) 26-09-16 e.a.*[3]	Waarschuwing: voorzichtigheid is geboden wanneer patiënten behandeld worden voor ademhalingsdepressie of in het geval van gelijktijdig gebruik van geneesmiddelen die het centraal zenuwstelsel onderdrukken of indien de aanbevolen dosering aanzienlijk wordt overschreden, omdat de mogelijkheid van ademhalingsdepressie niet uitgesloten kan worden in deze situaties. Bw: zelden: allergische reactie (b.v. dyspneu, bronchospasme, piepende ademhaling, angioneurotisch oedeem), ademhalingsdepressie, dyspnoe. Als de aanbevolen dosering aanzienlijk overschreden is en andere centraal depressieve stoffen gelijktijdig zijn toegediend, kan ademhalingsdepressie voorkomen. Een verslechtering van astma is gemeld, al is geen causaal verband vastgesteld.

ref. 11 SPC Diacetylmorfine (diamorfine) 30-05-16	CI: ernstige ademdepressie, exacerbatie van chronisch obstructieve longziekte (COPD). Waarschuwing: Voorzichtigheid is geboden bij het behandelen van patiënten met milde tot matige ademdepressie of obstructieve longziekte, omdat Diacetylmorfine deze aandoeningen kan verergeren. Bw: vaak: pneumonie, astma, dyspneu, hoesten; onbekend: ademstilstand, onderdrukte ademhaling.
ref. 12 SPC Abstral (fentanyl) 29-07-16 e.a.*[4]	CI: ernstige ademhalingsdepressie of ernstige obstructieve longaandoeningen. Waarschuwing: Net zoals bij alle opioïden bestaat het risico op klinisch significante ademhalingsdepressie gerelateerd aan het gebruik van Abstral. Bijzondere voorzichtigheid is geboden tijdens de dosistitratie van Abstral bij patiënten met chronische obstructieve longziekten of andere medische aandoeningen die kunnen leiden tot ademhalingsdepressie (bijv. myasthenia gravis) vanwege het risico op verdere ademhalingsdepressie, die kan leiden tot respiratoire insufficiëntie. Bw: vaak: dyspneu; onbekend: onderdrukte ademhaling.
ref. 13 SPC Palladon (hydromorfon) 12-01-2017 e.a.*[5]	CI: ademhalingsdepressie. Waarschuwing: Bij overmatig gebruik van opioïden is ademhalingsdepressie een groot risico. Bw: soms: dyspnoe; zelden: ademhalingsdepressie, bronchospasmen.

*[1] Sufenta (sufentanil) 09-12-16
*[2] Vergelijkbare informatie in Methadon HCl Apotex 08-01-2015, MorZet (nicomorfine) 16-11-11, Pethidine 05-10-11, Dipidolor (piritramide) 24-03-17.
*[3] Vergelijkbare informatie in Nalbufine HCl Orpha 11-04-11, Ultiva (remifentanil) 10-05-17.
*[4] Vergelijkbare informatie in Palexia Retard 07-07-16.
*[5] Vergelijkbare informatie in SPC MS Contin (morfine) 13-02-2017, Oxycontin (oxycodon) 01-06-16.

RISICOFACTOREN EN INCIDENTIE

Risicofactoren	-
Incidentie	-

	Contra-indicatie	**Actie**	**Datum**
Beslissing deskundigen	Nee	Nee	15-11-2017