Evidence Table 20. Managing Exacerbations: Heliox

Abbreviations used in table:

CI	**confidence interval**
ED	**emergency department**
FEV_1	**forced expiratory volume in 1 sec.**
H	**helium-oxygen (heliox)**
ICS	**inhaled corticosteroid**
O	**oxygen**
OR	**odds ratio**
PEF	**peak expiratory flow**
PEFR	**peak expiratory flow rate**
PI	**pulmonary index**
RCT	**randomized control trial**
RR	**relative risk**
SMD	**standardized mean difference**
WMD	**weighted mean difference**

*** indicates primary outcome**

Evidence Table 20. Managing Exacerbations: Heliox

Citation (Sponsor)	Study Design	Purpose/ Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)	Treatment	Dose	Lung Function	Vital Signs/Cardiovascular/Clinical Laboratory Values	Severity/Admissions	Safety
Ho et al. Heliox vs. air–oxygen mixtures for the treatment of patients with acute asthma. Chest 2003;123(3):882–890.	Meta-analysis of studies published between 1966 and 2002	To evaluate the efficacy of heliox on respiratory mechanics and outcomes in patients with acute asthma	15 articles (8 randomized control trials (RCTs) (n ranged from 11 to 205), 1 nonrandomized prospective controlled trial (n=27), 1 retrospective case-match controlled trial (n=22), 4 before–after case series, and 1 case report)	Age: Months to 70 yr Gender: Not reported Ethnicity: Not reported	Acute asthma	Arm 1 Any mixture of helium and O with or without concurrent beta-agonists, para-sympatholytics and corticosteroids, and with or without invasive ventilation Arm 2 Oxygen (O)		There was no significant difference in PEF between interventions (WMD +3%, 95% CI –2% to +8%; 4 RCTs) within the first hour. The level of confidence was 92% that heliox provides a benefit as an adjunct to standard medical care in acute asthma. Based on weighted linear regression, patients with <43% PEF may benefit more from heliox vs. patients with less severe acute asthma. Overall, all studies showed results in favor of heliox except 1 RCT and 1 case series that showed no improvement, 1 RCT that showed possible detrimental effect, and 1 small RCT that was inconclusive.			
Rodrigo et al. Heliox for nonintubated acute asthma patients. Cochrane Database Syst Rev 2003;(4):CD002884.	Meta-analysis of studies published between 1966 and 2002	To determine the effect of the addition of heliox to standard medical care on the course of acute asthma, as measured by pulmonary function testing and clinical endpoints	6 RCTs with 369 acute asthma patients; 5 studies involved adults and 1 study dealt with children.	Age: Mean age of samples: 12.3, 28.5, 32.3, 32.5, 37.0, and 44.5	Patients with clinical diagnosis of acute asthma who were seen in emergency departments (EDs)	Arm 1 Helium-oxygen (H) Arm 2 Placebo (O or air)	Four trials used 70:30; 2 trials used 80:29	There were no group differences in pulmonary function (SMD=0.13, 95% CI –0.09 to 0.34) based on 4 studies with n=127.	Heliox produced greater increase in heart rate than oxygen/air (SMD=7.67, 95% CI 0.79 to 14.55). There was no difference in O saturation (SMD=0.04, 95% CI –1.10 to 1.09) based on 3 studies with n=97.	There was no difference in Borg dyspnea score (WMD= –0.11, 95% CI –1.27 to 1.04) based on 3 studies with n=81.	There was no difference in hospital admissions (relative risk (RR) 1.02, 95% CI 0.58 to 1.81) based on 4 studies with n=324.

Citation (Sponsor)	Study Design	Purpose/ Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)	Treatment	Dose	Duration of Active Treatment; Duration of Postintervention/Off-Treatment Followup	Lung Function	Severity/Admissions
Kim et al., Helium/oxygen-driven albuterol nebulization in the treatment of children with moderate to severe asthma exacerbations: a randomized, controlled trial. Pediatrics 2005;116(5):1127–1133. (Praxair Corporation)	Randomized, single-blind, controlled trial	To evaluate the efficacy of heliox versus O in driving continuous albuterol nebulization in children with moderate to severe asthma	31 (30)	Age 2–18 yr, mean = 7.4 yr Gender 50% male, 50% female Ethnicity 60% Black, 37% White, 3% not given	Moderate–to-severe asthma Patients presented to urban, pediatric ED Pulmonary index (PI) score of >8 out of 15; mean = 10.2 at entry Beta$_2$-agonist, 50% 1 hour before, 87% 24 hours before Corticosteroids, 87% in the past, 17% in past 4 weeks Inhaled steroids, 43% Other controller therapies, 33% Mean initial oxygen (O) saturation on room air, 92.3% Previous hospitalizations, mean = 2.3	Arm 1 Heliox via compressed gas association 280 regulator driven by pressure of 50 lb per square inch gauge (n=16; n=15 completers) Arm 2 O (n=15)	Flow of 16 L/min Flow of 10 L/min	All received 20 minutes of nebulized albuterol treatment (5 mg) driven by 100% O, and oral steroids followed by nebulized albuterol (15 mg/hour) by heliox or O using nonrebreathing face mask up to 3 hours or until ED discharge.	*The mean change in PI score from baseline to 240 minutes was 6.67 for heliox vs. 3.33 for O (p <0.001). At 125 minutes, heliox group showed clinically significant absolute mean PI improvement vs. O group (p <0.05) that was sustained at 150, 180, and 240 minutes.	67% of heliox group were discharged from ED compared with 33% of O group (p=0.07). 73% of heliox group were discharged from hospital in <12 hours vs. 33% in O group (p <0.05).
Lee et al. Beneficial effects of albuterol therapy driven by heliox versus by oxygen in severe asthma exacerbation. Acad Emerg Med 2005;12(9):820–827. (Kaohsiumg Veterans General Hospital, Taiwan)	Two randomized, double-blind, controlled trials (ED of a university-affiliated tertiary care medical center)	Trial 1: To compare the efficacy of albuterol therapy driven by heliox versus by O and determine factors that were associated with beneficial response to heliox-driven albuterol therapy	Trial 1: 80 (80)	Trial 1 Age 18–50 yr, mean = 34.6 yr Gender 27% male, 73% female Ethnicity Not reported Smoking 14% tobacco smoking	Trial 1 Asthma diagnosed by American Thoracic Society criteria History of reversible airway obstruction as manifested by episodes of cough, dyspnea, and wheeze interspersed with symptom-free periods; 35% with history of asthma admission and 6% with history of mechanical ventilation for asthma Pretreatment PEF <50%, mean = 35.2% pred. Infectious exacerbation, 47% Days of exacerbation before ED visit, mean = 2.9 days Ipratropium, 22.5%; beta$_2$-agonist, 72.5%; oral corticosteroids, 17.5%; inhaled corticosteroid (ICS), 42.5%; methylxanthine, 36%; antileukotriene, 17.5% Heart rate, mean = 100 beats/min (104 for heliox group, 97 for O group, p <0.01) Respiratory rate, mean = 25.5 breaths/min SpO_2, mean = 94.8%	Arm 1 Heliox (H) (n=40; n=40 completers)	Albuterol (2.5 mg) in 3 mL of 0.9% saline via a nebulizer powered by helium/oxygen 80%/20%	Trial 1 3 treatments with 15-minute washout periods	Trial 1 *Both groups improved in PEF (p <0.001) with increase in H approximately twofold those in O. After first treatment, PEF increased by 17.5% in O and 35.7% in H (p <0.005); after third treatment, PEF increased from baseline by 39.7% in O vs. 71.4% in H (p <0.01). More in H vs. O reached PEF >60% pred. at end of third treatment (OR 2.58, 95% CI 1.03 to 6.46). Age (p=0.035) and pretreatment PEF (p=0.010) were associated with response to heliox; respiratory rate (p=0.13), heart rate (p=0.544), and smoking status (p=0.170) were not associated.	Trial 1 There was no difference in admission rates (18/40 in O vs. 12/40 in H, p=0.16). Among those discharged from ED, shorter stay for H vs. O (76 min vs. 86 min, p=0.007)

Citation (Sponsor)	Study Design	Purpose/ Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)	Treatment	Dose	Duration of Active Treatment; Duration of Postintervention/Off-Treatment Followup	Lung Function	Severity/Admissions
Lee et al. Beneficial effects of albuterol therapy driven by heliox versus by oxygen in severe asthma exacerbation. Acad Emerg Med 2005;12(9):820–827. (Kaohsiumg Veterans General Hospital, Taiwan)	Two randomized, double-blind, controlled trials (ED of a university-affiliated tertiary care medical center)	<u>Trial 2</u> To compare the efficacy of albuterol therapy driven by heliox versus by O in older patients	Trial 2: 80 (80)	<u>Trial 2</u> Age: >40 yr, mean = 54 yr Gender: 35% male, 65% female Ethnicity: Not reported Smoking: 12.5% tobacco smoking	<u>Trial 2</u> Asthma diagnosed by American Thoracic Society criteria History of reversible airway obstruction as manifested by episodes of cough, dyspnea, and wheeze interspersed with symptom-free periods; 35% with history of asthma admission and 6% with history of mechanical ventilation for asthma Pretreatment PEF<40%, mean = 26.4% pred. Baseline FEV_1 % pred., mean = 35.4 Ipratropium, 14%; $beta_2$-agonist, 84%; systemic corticosteroids, 17.5%; ICS, 42.5%; methylxanthine, 29%; antileukotriene, 15% Heart rate, mean = 95 beats/min Respiratory rate, mean = 23.5 breaths/min SpO_2, mean = 95.4%	Arm 2 Oxygen (O) (n=40; n=40 completers)	Albuterol (2.5 mg) in 3 mL of 0.9% saline via a nebulizer powered by air, O	<u>Trial 2</u> 2 treatments with 15-minute washout periods	<u>Trial 2</u> Improvement in PEF in H vs. O was greatest (23% pred.) for those in first quartile of pretreatment PEF (p <0.05). There were greater decreases in dyspnea score for H vs. O for those in lower 2 quartiles vs. upper 2 quartiles of pretreatment PEF.	
Rivera et al. Albuterol nebulized in heliox in the initial ED treatment of pediatric asthma: a blinded, randomized controlled trial. Am J Emerg Med 2006;24(1):38–42.	Blinded, randomized controlled trial (pediatric ED of a tertiary care, urban, university-based children's hospital)	To determine if delivery of continuous nebulized albuterol with heliox led to greater clinical improvement over nebulized albuterol delivered with O	41 (41)	Age: 3–16 yr, median 8 in heliox group, 7 in O group Gender: 61% male, 39% female Ethnicity: Not reported	Moderately severe asthma exacerbation with modified dyspnea index of 4 or higher on admission (median 6 for heliox group and 5 for O group, p=0.936) Previous history of at least 3 prior episodes of reversible bronchospasm	Arm 1 Heliox (H) (n=20; n=20 completers) Arm 2 Oxygen (O) (n=21; n=21 completers)	Continuous albuterol therapy (0.45 mg/kg, maximum dose 15 mg/h) delivered by nonrebreather face mask nebulized with helium/oxygen, 70%/30% Continuous albuterol therapy (0.45 mg/kg, maximum dose 15 mg/hour) delivered by nonrebreather face mask nebulized with air/oxygen, 70%/30%	All patients received 3 doses of aerosolized albuterol (2.5 mg/treatment given with 8 L of O), intravenous (IV) fluids at a weight-based maintenance rate, and 2 mg/kg IV methylprednisolone. After third albuterol treatment, they were randomized to H or O, with assessment at 10 and 20 minutes after randomization.		*Median modified dyspnea index scores improved for both groups, with no clinical (≥2 points) or statistical difference (p=0.169 after 10 minutes; p=0.062 after 20 minutes) between groups. Rate of admission was 60% for H and 81% for O (p=0.181).