



EM CASES SUMMARY

Episode 193 Life Threatening Asthma

With Drs. Leeor Sommer & Sameer Mal

Prepared by Sara Brade April, 2024

Recognition of life-threatening, near fatal asthma

- **Appearance:** Agitated, obtunded, few word dyspnea, accessory muscle use/ tripodding, respiratory arrest
- **Vitals:** hypoxic, increased (>30) or decreased RR, elevated HR (>120), bradycardia indicative of impending arrest
- **Physical exam:** silent chest, biphasic wheeze
- **Bedside investigations:** Peak flow <25% patient's best (*although there is no role for measuring peak flows in the crashing asthmatic*)
- **Clinical course:** Suboptimal/worsening response to initial therapies, fatiguing, decreasing LOC

Overview: Initial approach to management of the crashing asthmatic

Call for help

RNs/ RT/ another emerg doc/ ICU/ anaesthesia

B – C – A

Breathing THEN Circulation THEN Airway

Breathing

- **O2** via NP
- Immediate inhaled bronchodilators
 - Continuous **nebulized salbutamol**, up to 15 mg/hr
 - Continuous **nebulized ipratropium**, up to 1.5mg/hr
- **IV Methylprednisolone** 125 mg
- **IV Magnesium sulfate** 2 g over 10-15 mins, repeat x3; consider IV fluid bolus before giving magnesium because of hypotension risk and to replace insensible losses from asthma
- Systemic bronchodilators
 - **IM/IV Epinephrine**
 - IM: 0.3 to 0.5 mg q 20 mins x 1-2 doses
 - IV: ** preferred over IM ** initial 5 mcg/min, titrate up by 1-15 mcg/min every 2-3 mins, dose range: 0.05 to 0.5 mcg/kg/min, down titrate as soon as able

OR

- **IV Salbutamol**
 - Give after push dose or IM epi as an alternative to IV epi infusion

- IV: initial 2-5 mcg/min, titrate up every 15-30 mins max 20 mcg/min
- For the agitated/ tachypneic patient with severe increased work of breathing: Consider **IV ketamine** (25-50 mg IV bolus, 0.4-0.5 mg/kg, then 30 min infusion same dose) or **IV fentanyl** (75-150 mcg IV bolus, 1-2 mcg/kg, titrate to effect) to reduce tachypnea/ agitation/ anxiety and facilitate the use of other treatments/ NIV

Circulation

- Place as many peripheral IVs as possible
- IV crystalloid boluses to compensate for insensible losses and to avoid hypotension caused by magnesium/ hyperinflation
- Reducing respiratory rate/reversing dynamic hyperinflation will improve hemodynamics and increase preload

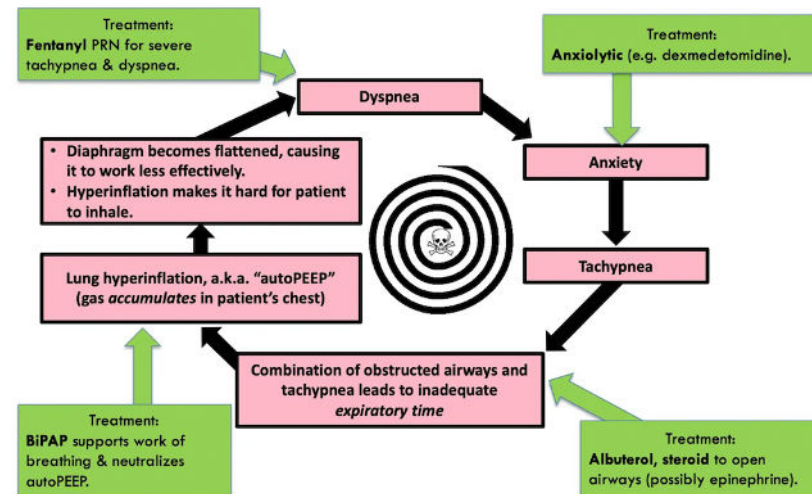
Airway

- BPAP or CPAP for tachypnea/ increased work of breathing/ hypoxia
- Consider ketamine or fentanyl to facilitate NIPPV in the agitated/ anxious patient
- Use NIPPV to avoid intubation in the obtunded patient who is maintaining airway protection
- Delay intubation if possible as there is a high risk for peri-intubation morbidity and mortality
- Will need intubation if respiratory arrest requiring BVM/ obtunded and not protecting airway

Breaking the vicious cycle of life-threatening asthma

The goal of our interventions is to get the patient out of the “vicious cycle” of severe asthma exacerbations. If tachypnea can be reduced and ventilation improved, the need for intubation can be prevented. In patients who are very tachypneic with severe work of breathing, adjuncts like ketamine or fentanyl can aid in tachypnea reduction and may facilitate improved delivery of bronchodilators/NIPPV.

Vicious Cycle of asthma exacerbation & how to break it



Asthma involves a vicious cycle of airway obstruction and dyspnea that leads to tachypnea. Asthmatics will be unable to exhale properly if they are breathing fast, so they can't tolerate tachypnea. Over time, this cycle will lead to diaphragmatic fatigue and exhaustion. Aggressive intervention before the point of exhaustion can generally avoid intubation.

-Internet Book of Critical Care, by @PulmCrit

Source: Internet Book of Critical Care

Medications for the crashing asthmatic / life-threatening asthma

Medication	Dose	Comments	Safety Considerations
Inhaled bronchodilators			
<ul style="list-style-type: none"> Salbutamol 	2.5-5 mg NEB x3 back-to-back OR Continuous NEB 15 mg/hr	Short-acting beta-agonist (SABA).	Causes tachycardia, hypokalemia, metabolic (lactic) acidosis.
<ul style="list-style-type: none"> Ipratropium 	0.5 mg NEB x3 back-to-back OR Continuous NEB 1.5 mg/hr	Short-acting muscarinic antagonist (SAMA).	NEB dose should be decreased after first hour to 0.5 mg/hr.

Systemic bronchodilators			
<ul style="list-style-type: none"> Epinephrine 	<p>IV push-dose: 5 mcg/dose q 2-3 mins</p> <p>IV infusion: initial 5 mcg/min, titrate up by 1-15 mcg/min every 2-3 mins, dose range: 0.05 to 0.5 mcg/kg/min, down titrate as soon as able.</p> <p>IM: 0.3 to 0.5 mg q 20 mins x 1-2 doses</p> <p>If this patient is obtunded with respiratory arrest requiring BVM, use AMAX4 algorithm dosing: 1 mcg/kg IV push q 30 seconds to 10 mins.</p>	<p>IV preferred over IM (greater ability to titrate, more predictable response).</p> <p>No high quality evidence.</p> <p><u>PUSH-DOSE IV EPI:</u> Take "code epi" (1 mg/10 ml). Draw up 1 ml (100 mcg) into a flush with 9cc of NS in it. You now have 10 mcg/ml push-dose epi.</p> <p><u>"DIRTY EPI DRIP":</u> Take 1 mg of epi. Inject it into a 1 L bag of NS. You now have a 1 mcg/ml solution for IV infusion.</p>	<p>Causes tachycardia, hypertension, hypokalemia, myocardial ischemia, metabolic (lactic) acidosis, arrhythmias.</p> <p>Needs cardiac monitor.</p>
<ul style="list-style-type: none"> Salbutamol 	Initial 2-5mcg/min IV, titrate up every 15-30 mins, max 20 mcg/min	Give after push dose or IM epi as an alternative to IV epi infusion.	<p>Causes tachycardia, hypertension, hypokalemia, myocardial ischemia, metabolic (lactic) acidosis, arrhythmias.</p> <p>Do not give if HR already >120.</p> <p>Needs cardiac monitor.</p>

Magnesium sulfate	2 g IV over 10 mins, repeat q 10 mins x3 Target total dose is 6 mg in first hour, then infusion of 4 g/hr.	Best effect if given early. We likely underdose magnesium. Magnesium can help to blunt arrhythmogenic effects of epinephrine. Limited and contradictory evidence in adults.	Causes hypotension. Give fluids to mitigate this risk.
Fentanyl	1-2 mcg/ kg IV (ie. 75-150 mcg), titrate to effect to normalize RR	Use for the tachypneic patient with increased work of breathing. Use to facilitate your other treatments. Use the respiratory rate suppression to increase expiratory time. This will hopefully decrease auto-PEEP and gas trapping. No high-quality evidence.	Do NOT give to patients who are already tiring/ decreased LOC.

Ketamine	Best evidence-based dose (single RCT) is 0.4-0.5 mg/kg IV (ie. 25-50 mg) bolus followed by infusion over 30 mins of same dose. Induction dose for intubation: 1-2 mg/kg IV push.	Use to facilitate NIV in the agitated patient with increased work of breathing/ tachypnea. Helps with bronchodilation and breaking the anxiety/ tachypnea induced hyperinflation. If giving ketamine, be prepared to intubate. Consider even lower doses, can cause exaggerated RR and hemodynamic effects in catecholamine depleted patients. No high-quality evidence.	Causes emesis, laryngospasm, bronchorrhea, hypertension.
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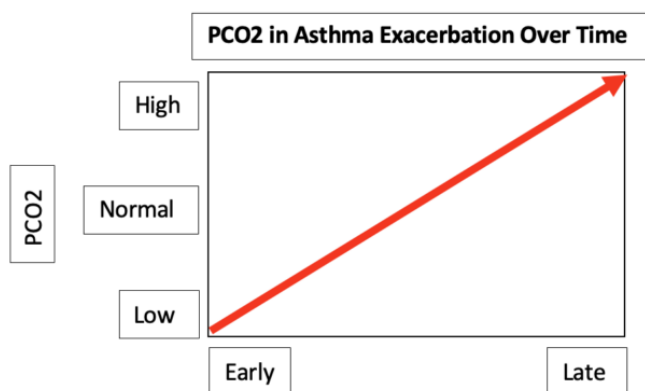
Pitfall: Avoid benzodiazepines. Some evidence suggests increased mortality in severe asthma. Treat the patient's anxiety by treating their underlying respiratory illness.

Why delay intubation as much as possible in severe asthma?

Dynamic hyperinflation with asthma results in tachypnea, anxiety, poor ventilation, increased intrathoracic pressure, and acidemia. Ultimately, this process leads to respiratory muscle fatigue, hypoxia, and encephalopathy. *Intubation is not a solution to the ventilatory problem of asthma.* A tube in the trachea actually worsens the underlying pathophysiology by increasing resistance to expiratory flow and by adding more dead space. Intubation is a supportive measure required for selected critically ill patients to buy time for our other treatments to work. Intubation in these patients is a high-risk procedure as they are most often hypoxic, acidotic, and tachypneic. Ventilating these patients is challenging and they are at risk for barotrauma and clinical deterioration.

The role of blood gases in the decision to intubate the patient with life-threatening asthma

Serial blood gas measurements may be helpful in determining a patient's clinical trajectory. A rising PCO₂ over time is a sign that the patient is fatiguing and may be progressing toward respiratory failure.



Early in the exacerbation, the patient's PCO₂ will be low secondary to tachypnea. Over time as the exacerbation becomes more severe and ventilation is compromised, the PCO₂ will start to rise. In the "middle" of the exacerbation, the PCO₂ will appear in the normal range which can be falsely reassuring.

The blood gas is just one data point that needs to be integrated into the clinical context. The decision to intubate a patient with a severe asthma exacerbation should not be made based on the blood gas alone, but a normal or rising PCO₂ should prompt careful clinical assessment for possible impending respiratory failure.

Ventilation strategies for the crashing asthmatic – indications and cautions

- Non-Invasive-Positive-Pressure-Ventilation (NIPPV) should be considered in patients with an elevated respiratory rate (>high 20s) and increased work of breathing
- CPAP or BPAP is preferred over HFNC, and CPAP is preferred over BPAP for patients with especially high respiratory rates who are unable to trigger the BPAP adequately due to the short inspiration phase
- Consider ketamine or fentanyl to facilitate the use of NIPPV
- Endotracheal intubation should be the last resort ventilation strategy
- Intubation is generally required for patients presenting with, or who have progressed to, respiratory arrest/ severely obtunded requiring BVM/ not protecting airway
- If endotracheal intubation is necessary, minimize the apneic period and use an obstructive ventilation strategy to avoid hyperinflation

The following tables include indications for and cautions using CPAP, BPAP, HFNC, endotracheal intubation and ventilation settings.

Method	Indication	Comments
<ul style="list-style-type: none"> CPAP (NIV) 	<p>Tachypneic/ working to breathe but NOT yet tiring.</p> <p>Start at 10 cmH2O, titrate to effect.</p>	<p>Stents open the airways during expiration to improve ventilation.</p> <p>Permissive hypercapnia to avoid intubation.</p> <p>Good evidence to help avoid intubation, but mostly extrapolated from COPD literature.</p> <p>CAUTION: Contraindicated if patient not protecting airway.</p> <p>Needs close monitoring of tidal volume/ minute ventilation.</p>
<ul style="list-style-type: none"> BPAP (NIV) 	<p>Patient starting to fatigue, some decreased LOC acceptable.</p> <p>Start at 10 cmH2O/ 5 cmH2O, titrate to effect.</p>	<p>Along with stenting airways during expiration, supplements the patient's work of breathing.</p> <p>Permissive hypercapnia to avoid intubation.</p> <p>Good evidence to help avoid intubation, but mostly extrapolated from COPD literature.</p> <p>CAUTION: Contraindicated if patient not protecting airway.</p> <p>Needs close monitoring of tidal volume/ minute ventilation.</p>
<ul style="list-style-type: none"> HFNC (NIV) 	<p>Patient not tolerating CPAP/ BPAP.</p> <p>CPAP/ BPAP/ intubation not within the patient's goals of care.</p> <p>Start at max flow rate 60 L/min. Titrate FiO2 to SpO2 90%.</p>	<p>Using HFNC not for high FiO2 but for high flow rates to get some possible airway stenting.</p> <p>Permissive hypercapnia to avoid intubation.</p> <p>If not tolerating HFNC after not tolerating CPAP/ BPAP, likely needs intubation.</p> <p>No high quality evidence.</p> <p>CAUTION: Needs close monitoring for deterioration.</p>

<ul style="list-style-type: none"> Intubation (Invasive MV) 	<p>Last line therapy when patient tiring/ failed max medical therapy/ NIV.</p> <p>Respiratory arrest/ severely depressed LOC and not protecting airway/ requiring BVM.</p>	<p>Preparation: Optimize positioning, HOB 30 degrees, face plane parallel with ceiling, ear and sternal notch aligned parallel to floor. Preoxygenate with NIV, keep nasal prongs on for apneic oxygenation, minimize apneic period, avoid bagging. FONA equipment available. Consider 1-2 amp bicarb push IV, fluid bolus IV +/- vasopressors pre-intubation.</p> <p>Method: RSI with large bore tube. Optimize first-pass success (ie. VL with bougie, most experienced intubator).</p> <p>Meds: ketamine 1-2 mg/kg IV push, immediately followed by rocuronium 1.5 mg/kg IV.</p> <p>"Bear hug"/ forced exhalation prior to connecting to the ventilator.</p> <p>VENT SETTINGS: Mode: PC or VC TV: For VC. 6-8ml/kg to ideal BW (based on height). If plateau pressure is alarming, titrate TV down to 4 ml/kg. IP: For PC. <35 mmHg Target plateau pressure is <35 mmHg. RR: 10 bpm I:E: 1:4 – 1:5 PEEP: 0-5 mmHg Insp flow rate: >100 L/min FiO2: Target SpO2 90%</p> <p>Once intubated, give bronchodilators through the circuit.</p> <p>CAUTION: HIGH RISK for peri-intubation morbidity and mortality.</p> <p>Should be avoided if at all possible with trials of NIV/ max medical therapy prior to intubation.</p>
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Rapid Sequence Intubation (RSI) pearls in the crashing asthmatic

- Have an epinephrine infusion ready to run (or push dose epinephrine drawn up) before intubation as hypotension is likely to occur when intubating the crashing asthmatic, as epinephrine is an ideal drug to correct hypotension in this scenario.
- Allow the patient to sit upright for as long as possible during the peri-intubation period to allow for best possible ventilation
- When performing endotracheal intubation in the crashing asthmatic, during the shortest possible apneic period, have the patient maintained on nasal prongs at 15L and avoid BVM whenever possible
- A long expiration time is necessary to prevent dynamic hyperinflation
- Allow *permissive hypercapnia* and *permissive acidemia* along with an *obstructive ventilation settings strategy* as outline in the above table

Stepwise approach to the crashing intubated asthmatic – DOPES mnemonic

Peri-intubation complication rate in this situation is very high. We need a checklist approach to ensure thorough evaluation and management in this case. You can use the **DOPES mnemonic** to guide this assessment. Have a partner perform this checklist with you to ensure no errors are made.

1.D: Is the tube Dislodged?

- Put the VL in the mouth and visualize the tube. Make sure the cuff hasn't herniated, make sure the tube is in the trachea. Reposition tube if dislodged.
- Reassess for clinical improvement.

2.O: Is the tube Obstructed?

- Pass a suction catheter through the tube and suction.
- Reassess for clinical improvement.

3.P: Is there a Pneumothorax?

- Look for asymmetric chest excursion, auscultate the lungs, palpated for crepitus, POCUS for pneumothorax.
- Manage pneumothorax, if present.
- Reassess for clinical improvement.

4.E: Is there a problem with the Equipment/circuit?

- Disconnect the vent, inspect and test each part of the circuit (ie. tubing, O2 supply, PEEP valve, all connections). Ensure no breaches in the circuit.
- Replace any faulty part, if found.
- Reassess for clinical improvement.

5.S: Is there breath Stacking?

- Optimize vent settings.
- Disconnect from vent and "bear hug"/ forced exhalation, then reconnect.
- Reassess for clinical improvement.

Advanced therapies for the intubated asthmatic who is not improving

Options include:

- Optimizing ventilator settings with assistance from your ICU colleagues
- Involving anaesthesia to trial inhaled anaesthetic gases
- ECMO for refractory acidemia/ hypoxia.

For further learning on the crashing asthmatic, watch Dr. Mike Betzner in his [talk from EMU on the crashing asthmatic](#)

EM Cases Emergency Treatment Algorithm for the Crashing Asthmatic

PUSH DOSE IV EPI:
Take "candy epi" (1 mg/10 ml). Draw up 1 ml (100 mcg) into a flush with Sec of NS in it. You now have 20 mcg/ml push-dose epi.

"DIRTY EPI DRIP":
Take 1 mg of epi. Inject it into a 1 L bag of NS. You now have a 1 mcg/ml solution for IV infusion.

AVOID BENZOS IN ASTHMA, ASSOCIATED WITH INCR MORTALITY.

Call for help (RN/RT/second ED MD/ ICU anaesthesia)
NP O2

Immediate inhaled bronchodilators:
Salbutamol 5 mg NEB x3 B2B, OR 15 mg/hr
Ipratropium 0.5 mg NEB x3 B2B, OR 1.5 mg/hr in 1st hr, then 0.5 mg/hr
Fluid bolus IV
Methylprednisolone 125 mg IV
Magnesium sulfate 2 g IV over 10-15 mins, repeat x3 in 1st hr

Systemic bronchodilators:
Ipratropine IM/IV
• IM: 0.5 to 0.5 mg q 30 mins x 1-2 doses.
• IV push-dose: 5 mcg/dose q 2-3 mins.
• IV infusion: ** preferred over IM ** initial 5 mcg/min, titrate up by 1-15 mcg/min every 2-3 mins, dose range: 0.05 to 0.5 mcg/kg/min, down titrate as soon as able.

OR
Salbutamol IV
• Give after push dose or IM epi as an alternative to IV epi infusion.
• IV: Initial 2-5 mcg/min, titrate up every 15-30 mins max 20 mcg/min.

Consider fentanyl IV in tachypneic patients (75-150 mcg bolus, 1-2 mcg/kg, titrate to RR), to increase expiratory time.

Think about Ddx. Make sure severe asthma is the correct diagnosis.

- Anaphylaxis (3-4% of severe asthma exacerbation meets criteria for anaphylaxis)
- Pulmonary embolism
- FB aspiration
- Upper airway obstruction
- Pneumothorax
- Heart failure
- Vagal cord dysfunction
- Pneumonia

BWARE OF NORMAL PCO2, MAY MEAN PATIENT IS TIRING

AGITATED TACHYPNEIC INCREASED WORK OF BREATHING

CPAP to optimize exhalation (10 cmH2O, titrate up).

Consider low-dose ketamine to facilitate NIV/ for bronchodilation.

Ketamine: 25-50 mg bolus IV (0.4-0.5 mg/kg), then same dose infusion over 30 mins.

Ketamine can have exaggerated effects in critical illness even with low doses. Be prepared to INTUBATE.

TIRING BUT PROTECTING AIRWAY

BPAP to supplement WOB and optimize exhalation (10cmH2O / 5cmH2O, titrate up).

Consider low-dose ketamine to facilitate NIV if patient not tolerating. See ketamine dose to the left, may want to use even lower dose if already tiring.

SEVERELY OBTUNDED/ RESP ARREST NOT PROTECTING AIRWAY REQUIRING NIV

AMAX4

- A** ADRENALINE (1mg IV push over 1-2 mins)
- M** MUSCLE RELAXANT (3mg atrovicur 10ml over 1-2 mins)
- A** AIRWAY (2-4 mg atropine IV over 1-2 mins)
- X** EXTREME VENTILATION (TRA BRONCHODILATORS (200-400mcg IV), CONSIDER PNEUMOTHORAX)
- 4** 4 MINUTES TO HYPOXIC BRAIN INJURY

Continuous nebulized bronchodilators through the circuit.

Consider HFNC if not tolerating CPAP/ BPAP and NOT clinically requiring intubation or if CPAP/ BPAP/ intubation not within GOC. Start at max flow rate 60L/min, target SpO2 90%.

FAIL TO IMPROVE VENTILATION + OXYGENATION WITH NIV/ RESPIRATORY ARREST

PROCEED TO INTUBATION WITH CAUTION
See AMAX4 Algorithm.

Preparation	Positioning, preoxygenate with NIV, NP for apneic oxygenation, minimize agonic period, avoid bagging, FONA equipment available. Consider 1-2 amp bicarb IV push, IV fluid bolus, +/- vasopressors pre-intubation.
Method	RSI with large tube. Optimize first attempt success. Most experienced intubator. VL with bougie.
Meds	Ketamine: 1-2 mg/kg IV push, followed immediately by Rocuronium: 2.5 mg/kg IV push
Vent Settings	VENT SETTINGS: Mode: PC or VC TV: For VC: 6-8ml/kg to ideal BW (based on height). If plateau pressure is alarming, titrate TV down to 4 ml/kg. IP: For PC: <35 mmHg Target plateau pressure is <35 mmHg RR: 10 bpm I:E: 1:4 - 1:5 PEEP: 0-5 mmHg Insp flow rate: >100 l/min FIO2: Target SpO2 90%
Post-intubation	Usual management: verify tube placement, portable CXR, post-intubation sedation/ analgesia. Asthma-specific: Forced exhalation/ bear hug before connecting to circuit. Minimize bagging before connecting to circuit as risk of severe gas trapping/ pneumothorax. Once intubated, give continuous bronchodilators through circuit.

If the patient is still crashing, see right for vent troubleshooting.

CRASHING DESPITE VENT TROUBLESHOOTING

Call for help: ICU/ RT to help optimize the vent settings, anaesthesia for inhaled anaesthetic gases, consult/ transfer for ECMO for refractory hypoxia/ acidosis.

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References

1. Akenroye, A. T., Ajala, A., Azimi-Nekoo, E., & de Vos, G. S. (2018). Prevalence of anaphylaxis among adults admitted to critical care for severe asthma exacerbation. *Emergency Medicine Journal*, 35(10), 623-625.
2. Bond, K. R., Horsley, C. A., & Williams, A. B. (2018). Non-invasive ventilation use in status asthmaticus: 16 years of experience in a tertiary intensive care. *Emergency Medicine Australasia: EMA*, 30(2), 187–192.
3. Denmark, T. K., Crane, H. A., & Brown, L. (2006). Ketamine to avoid mechanical ventilation in severe pediatric asthma. *The Journal of Emergency Medicine*, 30(2), 163–166.
4. Emerman, C. L., & Cydulka, R. K. (1995). A randomized comparison of 100-mg vs 500-mg dose of methylprednisolone in the treatment of acute asthma. *Chest*, 107(6), 1559–1563.
5. Esmailian, M., Koushian Esfahani, M., & Heydari, F. (2018). The Effect of Low-Dose Ketamine in Treating Acute Asthma Attack; a Randomized Clinical Trial. *Emergency (Tehran, Iran)*, 6(1), e21.
6. Farkas, J. (2023). Asthma – EMCrit Project. EMCrit Project. <https://emcrit.org/ibcc/asthma/>
7. Goodacre, S., Cohen, J., Bradburn, M., Stevens, J., Gray, A., Bengler, J., & Coats, T. (2014). The 3Mg trial: a randomised controlled trial of intravenous or nebulised magnesium sulphate versus placebo in adults with acute severe asthma. *Health Technology Assessment (Winchester, England)*, 18(22), 1-168.
8. Hemming A, MacKenzie I, Finfer S. Response to ketamine in status asthmaticus resistant to maximal medical treatment. *Thorax*. 1994 Jan;49(1):90-1.
9. Kew, K. M., Kirtchuk, L., & Michell, C. I. (2014). Intravenous magnesium sulfate for treating adults with acute asthma in the emergency department. *Cochrane Database of Systematic Reviews*, (5).
10. La Via L, Sanfilippo F, Cuttone G, Dezio V, Falcone M, Brancati S, Crimi C, Astuto M. Use of ketamine in patients with refractory severe asthma exacerbations: systematic review of prospective studies. *Eur J Clin Pharmacol*. 2022 Oct;78(10):1613-1622.
11. Longrois, D., Conti, G., Mantz, J., Faltlhauser, A., Aantaa, R., & Tonner, P. (2014). Sedation in non-invasive ventilation: do we know what to do (and why)?. *Multidisciplinary Respiratory Medicine*, 9(1), 56.
12. Matsumoto, T., Tomii, K., Tachikawa, R., Otsuka, K., Nagata, K., Otsuka, K., Nakagawa, A., Mishima, M., & Chin, K. (2015). Role of sedation for agitated patients undergoing noninvasive ventilation: clinical practice in a tertiary referral hospital. *BMC Pulmonary Medicine*, 15, 71.
13. McKenzie, B. (2023). AMAX4 Algorithm. AMAX4 – LivetotheMax. <https://www.amax4.org/algorithm>.
14. Nakafero, G., Sanders, R. D., Nguyen-Van-Tam, J. S., & Myles, P. R. (2015). Association between benzodiazepine use and exacerbations and mortality in patients with asthma: a matched case-control and survival analysis using the United Kingdom Clinical Practice Research Datalink. *Pharmacoepidemiology and Drug Safety*, 24(8), 793–802.
15. Peberdy MA, Callaway CW, Neumar RW, et al; American Heart Association. (2010) Part 9: post-cardiac arrest care: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2010;122(18)(suppl 3):S768-S786
16. Reddel, H. K., Bacharier, L. B., Bateman, E. D., Brightling, C. E., Brusselle, G. G., Buhl, R., ... & Boulet, L. P. (2022). Global Initiative for Asthma Strategy 2021: executive summary and rationale for key changes. *American Journal of Respiratory and Critical Care Medicine*, 205(1), 17-35
17. Resuscitation Council UK. (2021). Emergency treatment of anaphylactic reactions: Guidelines for healthcare providers. Resuscitation Council UK. <https://www.resus.org.uk/library/additional-guidance/guidance-anaphylaxis/emergency-treatment>
18. Rock, M. J., Reyes de la Rocha, S., L'Hommedieu, C. S., & Truemper, E. (1986). Use of ketamine in asthmatic children to treat respiratory failure refractory to conventional therapy. *Critical Care Medicine*, 14(5), 514–516
19. Stojak, B. J., Halajian, E., Guthmann, R. A., & Nashelsky, J. (2019). Intravenous magnesium sulfate for acute asthma exacerbations. *American Family Physician*, 99(2), 127-128.
20. Strube PJ, Hallam PL. Ketamine by continuous infusion in status asthmaticus. *Anaesthesia*. 1986 Oct;41(10):1017-9.
21. Talbot, T., Roe, T., & Dushianthan, A. (2024). Management of Acute Life-Threatening Asthma Exacerbations in the Intensive Care Unit. *Applied Sciences*, 14(2), 693.