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Perioperative management of asthmatic patients

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INTRODUCTION

According to The World Health Organization asthma is a major non communicable disease, affecting both adults and children [1]. In 2019 it was estimated that it affected 262 million people and caused 461000 deaths [1]. A lot of asthmatic patients require some type of surgical procedure in their lives, and it is at this stage where the disease should be optimised [2].
Studies have showed the prevalence rate and severity of asthma is increasing worldwide, with variations among different countries ranging from 0.7% to 18.4% [3,4].
Most deaths related to asthma occur in low- and middle-income countries, because there is a challenge of under diagnosis and under treatment [1,8]. The Global Initiative for Asthma (GINA) has evidenced based strategy reports that are issued every two years with the aim to improve the diagnosis, management, and prevention of asthma [11].
Patients with asthma are at an increased risk of perioperative morbidity and mortality, because of bronchospasm and hypoxemia [5]. This pose a challenge for the anaesthetist in the perioperative period [3].

DEFINITION

According to the global initiative of asthma. It is a heterogeneous disease, characterized by chronic airway inflammation [1]. Defined by history of respiratory symptoms like a wheeze, shortness of breath, chest tightness plus a cough, that vary over time and intensity, together with variable expiratory airflow limitation [1,6].

CAUSES [1,6,8]

- Genetic predisposition and environmental factors play a major role.
- Airborne environmental exposures- Tobacco smoke, Pollutants, Ozone
- Atopic conditions and sensitization

PATHOPHYSIOLOGY

It is a combination of a genetic predisposition and environmental exposure. Inflammation occurs in the lower airways [6,8]. Most of these patients have type II inflammation which is associated with cytokines like: Interleukin (IL-4, IL-5, IL-13), and inflammatory cells (Eosinophils, mast cells, type II helper cells, basophils, immunoglobin E producing plasma cells and lymphocytes) [6].
The chronic inflammatory process causes tissue injury and subsequent airway structure remodeling [6,8]. Pathological alterations occur in the lower airways, primarily the mucosa and submucosa. Changes in the mucosa are that of epithelial hyperplasia and metaplasia of goblet cells, associated with an increase in mucus production [6]. There is also submucosa- smooth muscle hypertrophy, collagen deposition and large mucous glands domination. This leads to a formation of narrower airways and increased mucous production [6,8].
The obstruction that occurs is mainly bronchial because of mucus production and tissue oedema as well as smooth muscle constriction. Figure 1 below demonstrates airway structure remodeling [7]. Reversible airflow obstruction is an important factor for diagnosing asthma [6]. Clinicians must keep in mind that symptoms tend to be worse at night [6].

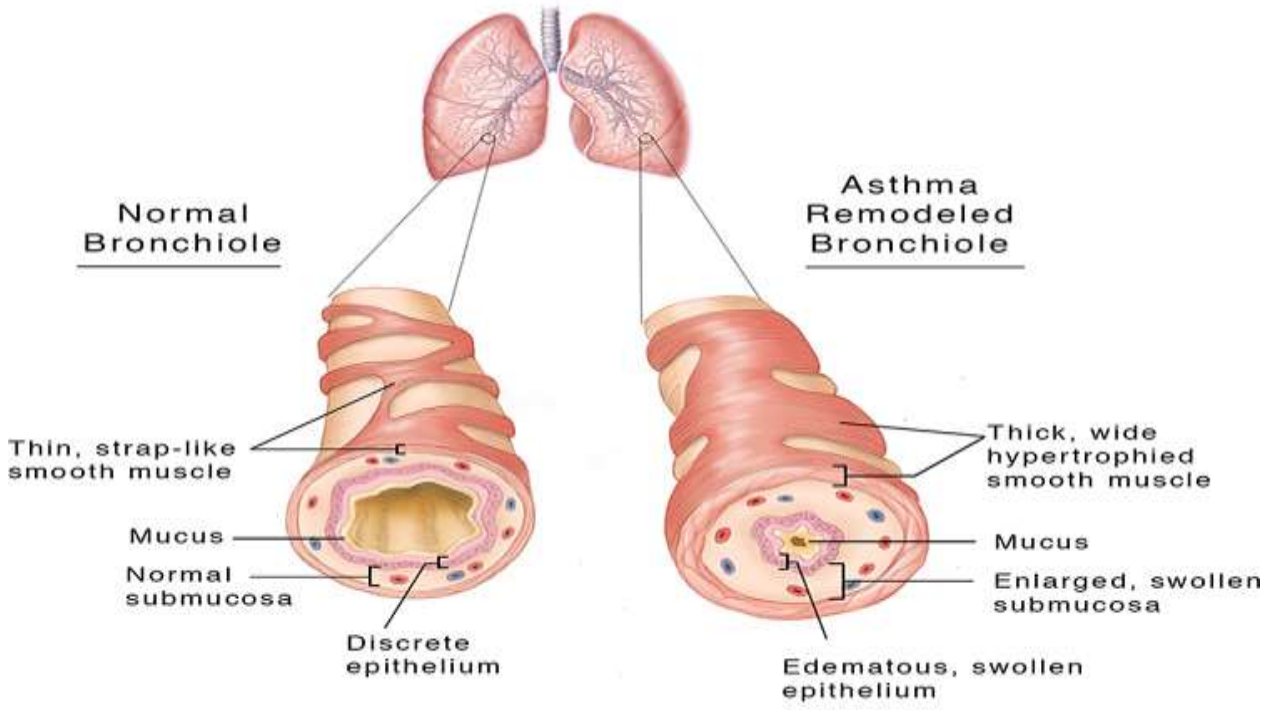

Figure 1: Chetty A, Nielsen HC. Targeting Airway Smooth Muscle Hypertrophy in Asthma. J Asthma Allergy. 2021;14:539-56

Triggers of asthma [1,5,6]

- Upper and lower respiratory tract infections
- Environmental pollutants as mentioned above
- Change in temperature
- Excitement
- Stress
- Exercise
- Allergens

CLASSIFICATION OF ASTHMA

This is done based on severity of asthma and is useful in making decisions for management when the clinician assesses the patient at the initial visit.
Figure 2 below is from a review by Bayable S.D, et al. showing how asthma is classified, and figure 3 is according to the GINA guidelines, looking at the frequency of symptoms [1,5].

Assessment of severity of asthma.

Clinical assessment	Well controlled	Not well controlled	Poorly controlled
1. Symptoms (wheezing, shortness of breath, chest tightness)	≤2 days/ week	>2 days/week	Daily
2. Night time awakenings with breathing problems	≤2 x/ month	3–4 x/month	>1 x/week
Short-acting beta 2 agonist use for rescue	≤2 days/ week	>2 days/week but not daily	Daily
Interference with normal activity	None	Some limitation	Extreme limitation
Exacerbations requiring systemic corticosteroids	≤1 x/year	2–3 x/year	>3 x/year
Patients above 5 years include additionally			
FEV1 predicted	>80%	60–80%	<60%
FEV1/FVC	>0.8	0.75–0.80	<0.75

Figure 2: Bayable S.D et al. Annals of Medicine and Surgery 2021.

Classification of asthma severity

	Frequency of symptoms Day	Night	% predicted FEV_1/PEFR	Variability PEFR%
Intermittent	<1/wk	≤2/m	≥80%	<20%
Mild persistent	≥1/wk <1/day	>2/m	≥80%	20-30%
Moderate persistent	Daily	≥1/wk	60-80%	>30%
Severe persistent	Daily	Frequent	≤60%	>30%

Classified according to the Global Initiative for Asthma [GINA] guidelines

Figure 3

RECENT TREATMENT GUIDELINES

The Global Initiative for Asthma 2021 guidelines has categorized medication for asthma into three; based on emerging evidence [11].

Categories of asthma medication [1,11]

1. **Controller medication (Inhaled steroids)**
    - Used to reduce airway inflammation
    - For symptom control
    - For reduction of exacerbation episodes
2. **Reliever medication (Short acting Beta agonists)**
    - When there is a need for relief of breakthrough symptoms
    - Used short term for Exercise induced bronchoconstriction
      Reducing the need for reliever treatment is an important goal and a measure for successful asthma treatment.
3. **Add on therapy for patients with severe asthma include**
    - Short course of oral corticosteroids plus high dose inhaled corticosteroids, or medium dose inhaled corticosteroids plus long-acting beta agonist.

   This category can be considered when patients have persistent symptoms, or exacerbations despite being optimized on treatment.

Initial controller treatment
Low dose inhaled corticosteroids are used for all patients with asthma. Once control has been maintained for 2-3 months; treatment can be stepped down to find the patients minimum effective treatment [1,11].
If a patient has persistent uncontrolled symptoms or exacerbations; one should assess if the treatment is applied correctly, and also inquire on the following:

- Inhaler technique
- Poor adherence
- Persistent exposure to allergens
- Co-morbidities
- Incorrect diagnosis

PERIOPERATIVE ASSESSMENT

The perioperative assessment is key to successful management. However, a practitioner can be misled by the variable nature of the disease as the symptoms can be completely absent before the surgical procedure [2]. The purpose of perioperative assessment is to determine the respiratory dysfunction and its magnitude, look at how effective the current treatment is, and prepare the patient for a suited anaesthetic technique [5,8].
The history taking should focus on the daily living activities, physical status, presence of infection, triggering factors and medication used [1,2,8].
Asthmatic patients with present symptoms that are poorly controlled; being the history of frequent exacerbations or hospital admissions, are at risk of perioperative respiratory problems. These respiratory problems are bronchospasm, sputum retention, atelectasis, infection, and respiratory failure. Elective surgery should be scheduled when asthma is well controlled to minimize perioperative respiratory adverse events [5,10].

Indicators of disease severity [1,9-11]

- History of frequent exacerbations
- The number of hospital visits
- Recent tracheal intubation and mechanical ventilation to manage a severe attack

- Prior perioperative exacerbations
- Therapy regime that the patient is on
- Recent respiratory tract infection
- Change in cough or sputum

Examination

The clinician must focus on detecting signs of acute bronchospasm, or an active lung infection, and these should motivate one to postpone an elective surgery procedure until the patient is clinically optimized [5,10]. It is important to also look for signs of a chronic lung disease and right heart failure [5].
If the patient is found to be wheezing preoperatively; this is a predictive sign for a difficult perioperative course [5].

Investigations

1) **Pulmonary function test**

Performing this test is guided by history and physical examination. The formal pulmonary function test helps to identify the severity of the disease, to determine whether the air flow obstruction is partially reversible after the use of a bronchodilator. Reversibility is indicated by an increase of 12% on FEV1 from base line, and an increase in FEV1 of greater than 200 ml in adults [5,12,13]. However normal values do not guarantee an uncomplicated perioperative course [5].

2) **Arterial blood gas**

ABG is an important test during an asthmatic attack but can be normal at base line.
During an acute asthmatic attack, early stages of bronchospasm make a patient hyperventilate and causes respiratory alkalosis [2,8].
A normal Paco2 in an acute asthmatic attack is an ominous sign that patient is eminent to decompensation, and action should be taken before further deterioration occurs. It is a sign that the patient is getting fatigue from increased work of breathing [2].

3) **ECG**

Changes will show [5]:

- Right atrial or ventricular hypertrophy
- Acute strain
- Right axis deviation
- Right bundle branch block

4) **Chest XR**

Signs of hyper-inflation may be seen. One must check for pulmonary congestion, oedema, or infection, and rule out pneumonia and heart failure [3,5].

Pre-operative pharmacological optimization

B2- adrenergic agonists, together with corticosteroids are essential to improve peri-operative lung function, and to reduce the incidence of post tracheal intubation wheeze [5]. To improve endobronchial cilia function and mucus clearance, patients booked for elective procedures should stop smoking 6-8 weeks before anaesthesia [5,14].

ANAESTHESIA

Pre-Medication

Midazolam 0.5mg/kg is effective in alleviating anxiety induced bronchospasm. It improves work of breathing as well. This drug should not be given to patients at risk of upper airway obstruction [5,14,15].

A prospective randomized double blinded study showed that administration of 1.5mg/kg - 2mg/kg IV lidocaine 90 s before laryngoscopy effectively suppressed the cough reflex and attenuates increases in the heart rate and mean arterial pressure [5,16].

Anaesthetic technique

Airway instrumentation should be avoided if possible and regional anaesthetic techniques should be considered if indicated. If a general anaesthetic cannot be avoided, then a laryngeal mask should be the first option if not contraindicated [2,5].
S. Kim and MS Bishop demonstrated that tracheal intubation caused an increase in the respiratory system resistance that can be reversed with bronchodilators, compared to the use of a laryngeal mask [17].

Choice of the anaesthetic drugs

Propofol

This is the drug of choice in a hemodynamically stable patient. It has the ability to attenuate the bronchospastic response to intubation on both asthmatic and non- asthmatic patients [5,18-20].
Studies have shown that; this drug compared to thiopental and etomidate, was associated with decreased airway resistance [20].
It has been shown to have direct effect on airway smooth muscle by causing a reduction in intracellular calcium; by inhibiting calcium influx and release of intracellular stores. It also influences the parasympathetic nervous system (Dose dependent attenuation in the vagal nerve stimulation induced bronchospasm) [21].
Propofol also has immune regulatory effects (Inhibits elevation of cytokines, secreted by TH2 cells, also IL-4, IL-5). Relaxant effect occurs by acting on GABA A channels in the brain stem and GABA B channels on a preganglionic cholinergic nerves in the lungs. It also stimulates airway ciliary motility [21].

Ketamine

An ideal induction agent for hemodynamically unstable asthmatics due to its ability to produce direct smooth muscle relaxation and bronchodilatation without decreasing arterial pressure or systemic vascular resistance. It blocks NMDA receptor induced bronchoconstriction [5,21,22].

Neuromuscular blocking agents

Generally, neuromuscular blocking agents are the most common medications to cause allergic reactions in the operating theatre [23].
Vecuronium, rocuronium and cis-actracurium are safer to use. Actracurium and mivacurium causes a dose dependent histamine release and should be avoided on asthmatic patients [24].
Even though, suxamethonium can release low levels of histamine, it is of great use for the asthmatic patient that needs a rapid sequence induction in low resource settings without significant morbidity and mortality [5,25].

Volatile anaesthetic agents

They produce bronchodilatation through a decrease in cytoplasmic ionized calcium concentration, and a reduction in calcium sensitivity of airway smooth muscles. An effective therapeutic modality in status asthmaticus when conventional therapy has failed [24].
Only desflurane increases pulmonary resistance significantly at a higher mac values, therefore it is essential to avoid using it in patients with reactive airway disease [2,5,24].

Intraoperative monitoring

Consider an arterial line placement in high-risk patients for Paco2 monitoring, because as bronchospasm worsens the $EtCO_2$ and $PaCO_2$ gradient widens [25].

VENTILATION STRATEGIES FOR ASTHMATIC PATIENTS

Ventilation of asthmatic patients could be a very challenging task. One should focus on monitoring the ventilatory and airway mechanics such as:

- Tidal volumes
- Peak inspiratory and Plateau pressures
- Compliance
- Gas flows
- Respiratory wave forms
- I:E ratios

Considerations during ventilation are [2]:

- Patients' airway resistance
- Gas trapping and alveolar hyperinflation
- Permissive hypercapnia

Preferred mode of ventilation

Preset volume-controlled mode is preferred because with this mode; both peak inspiratory pressures plus plateau pressures can be measured, and also the delivered tidal volumes will not be influenced by a fluctuation in peak airway pressures secondary to a variation in a degree of a bronchospasm. It is prudent to prolong the expiratory time on the ventilator setting because a bronchospasm is associated with slow emptying of the alveoli. This will minimize PEEPi build up. [2,26]

The breath rate can be lowered down between 6-10 bpm, I:E ratio set to between 1:4 and 1:5.

Tidal volumes can be lowered to between 4-6 ml/kg.

One should remember that the above maneuvers can worse hypercapnia.

When all else fail, a clinician can manually decompress the chest, by disconnecting the circuit from the patient for about 20-30 seconds, while simultaneously squeezing the patient's chest inwards with hands over both axillary areas [26].

Permissive Hypercapnia

As mentioned above, CO2 retention is a danger for these patients. Trying to lower CO2 with ordinary maneuvers can lead into a vicious circle that can be detrimental to the patient's wellbeing [2]. Permissive hypercapnia is when one allows higher levels of PaCO2, provided that the PH is maintained at 7,2 [2,26].

DANGERS OF HYPER INFLATION

Dynamic hyperinflation begins when there is a reduction in expiratory flow that leads to incomplete exhalation of delivered tidal volumes. Higher levels of minute ventilation should be avoided because this will result into more hyperinflation and a further increase of physiological dead space; as there is alveolar over distention with compression of the underlying capillaries, and poor perfusion [5]. This effect will result in a rise on pulmonary resistance, an increase in right atrial pressures with poor venous return, and a decreased cardiac output [26,27].

Interpretation of ventilator graphics

Ways of determining a rising intrinsic peep in a pre-set volume mode

1. **End inspiratory volume (VEI)**
   One can keep a patient apneic for 20-40 seconds and measure the total volume of exhaled gas, if it is more than 20ml/kg then the patient is in danger of barotrauma or possible cardiopulmonary effects. With this method the patient needs to be completely relaxed, and it is not routinely used [2,26].

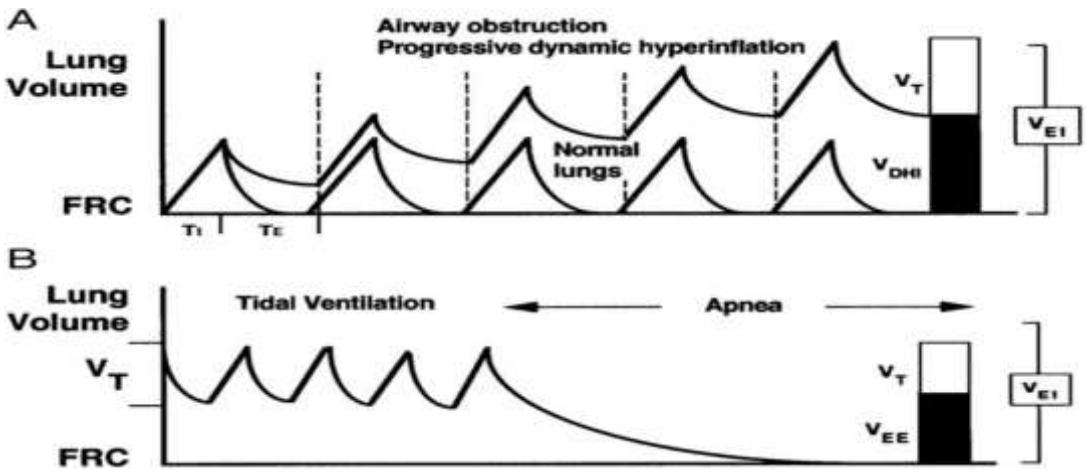

Figure 4: Dynamic hyperinflation on A. B showing measurements of VEI [27]

2. **Pressure time wave form in a volume pre-set mode**
   With the patient paralyzed one can initiate an end expiratory hold maneuver; observe an increase in pressure above the set PEEP, and that will be the intrinsic PEEP [26].

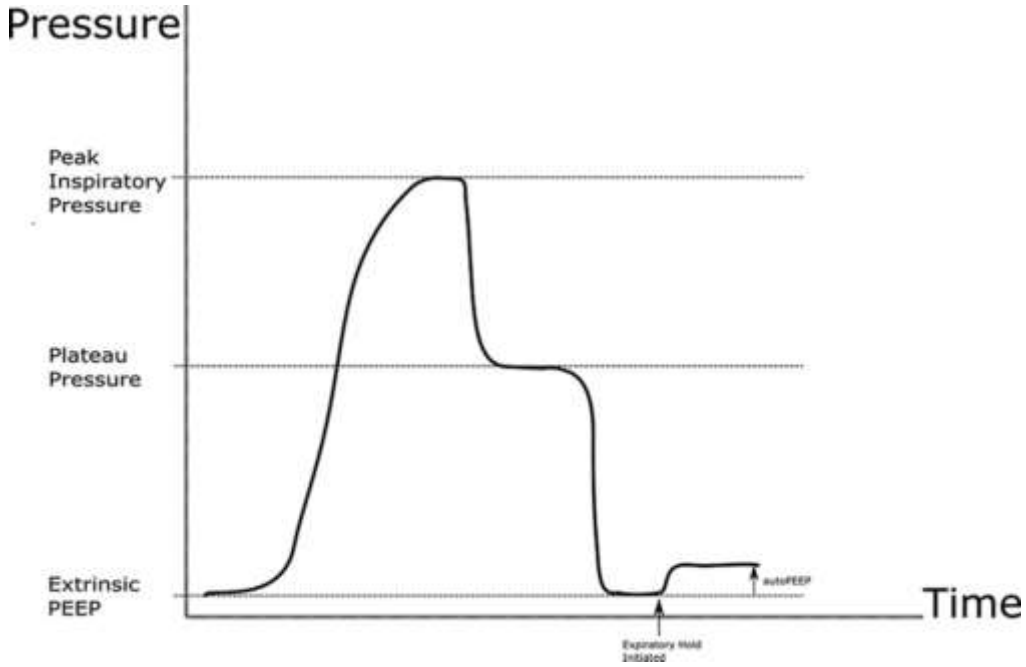

Figure 5: Determining the level of auto-PEEP on the pressure–time waveform in the volume pre-set ventilation mode by initiating an expiratory hold maneuver with the patient paralyzed [26]

3. **Flow time wave form in a volume pre-set mode**
   On this graphic one can observe failure of the expiratory flow to return to its base line before the initiation of the next breath [26].

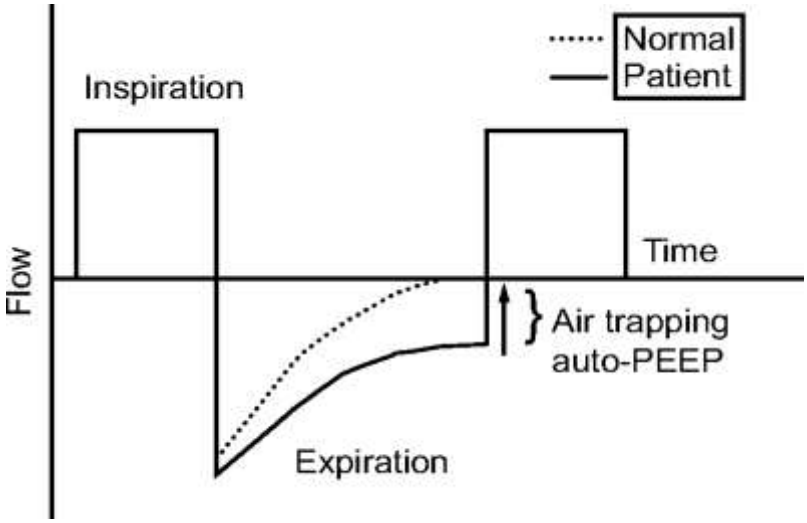

Figure 6 Flow-time waveform showing persistence of flow at end expiration in a patient with intrinsic positive end-expiratory pressure [PEEPi]. [29]

4. **Pressure time wave**
   On this wave form one can observe an increase in both peak inspiratory pressures and plateau pressures, without a change in their gradient.

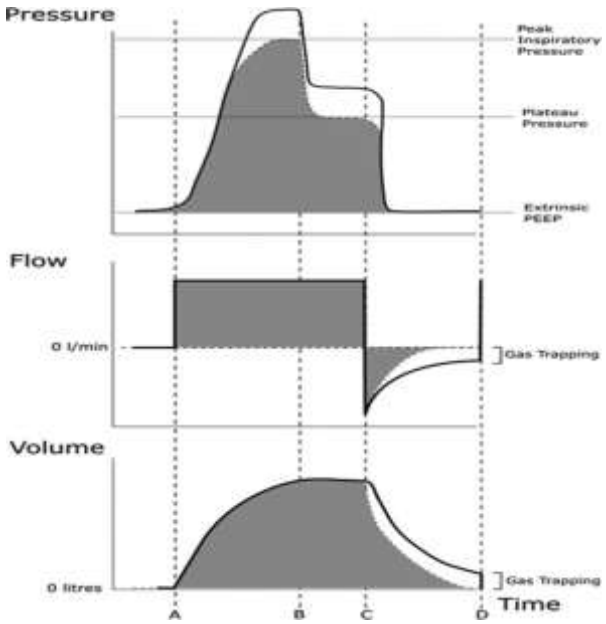

Figure 7: Identifying auto-PEEP (gas trapping) on the volume preset ventilator mode using ventilator graphics. The top image is Pressure–time wave form: Note the increase in PIP and Pplat with no change in the PIP- Pplat gradient. This change is also noted with the presence of a pneumothorax.
Middle image: Flow–time waveform: Note the prolonged expiratory phase with failure of air flow to return to baseline before the next breath is initiated.
Bottom image: Volume–time waveform: Note the prolonged expiratory phase with gas trapping manifesting as the failure of the expiratory volume to return to baseline (shaded area ¼ normal expiration). PEEP denotes positive end-expiratory pressure; PIP, peak inspiratory pressure; Pplat, plateau pressure. [26]

A difference in both inspiratory and expiratory volumes can be observed, provided that there are no leaks in the circuit or the ventilator.

Extra-PEEP in severe asthma

If an extra peep level is too low then can lead to small airway collapse and air trapping, whereas a high extra-PEEP level could cause further lung hyperinflation and circulation compromise [30]. Electrical impendence tomography (EIT) is a non- invasive radiation imaging tool that could provide dynamic information on ventilation and lung volumes under different clinical conditions [30,31].

A systematic literature review was conducted in PubMed after 2 articles reported using EIT. The review showed that a unified extra-PEEP is suggested to offset the initial airway closing pressure during mechanical ventilation for severe asthma [30].

MANAGEMENT OF AN INTRAOPERATIVE BRONCHOSPASM

Bronchospasms can occur at any stage of anaesthesia (Induction, Maintenance, or emergence) [25,28]. It is important to recognize it when occurring and start treatment promptly.

Signs of bronchospasm during IPPV [5,28,32]

- Increased peak airway and plateau pressures
- Decreased tidal volumes
- An associated expiratory wheeze on auscultation
- With a severe bronchospasm the chest might be silent
- Delayed rise in end tidal carbon dioxide, producing a characteristic shark fin appearance

Possible triggers of bronchospasm in theater [5]

- Airway instrumentation
- Drugs
- Allergic reaction
- Aspiration of gastric contents

Differential diagnosis [5]

- Partial obstruction of an ETT
- Pulmonary oedema
- Gastric contents aspiration
- Tension pneumothorax
- Foreign body in a tracheal bronchial tree

Ways to trouble shoot a high- pressure alarm

The clinician needs to determine if a sudden rise in pressure is because of a rise in airway resistance or a deterioration in pulmonary compliance [26].

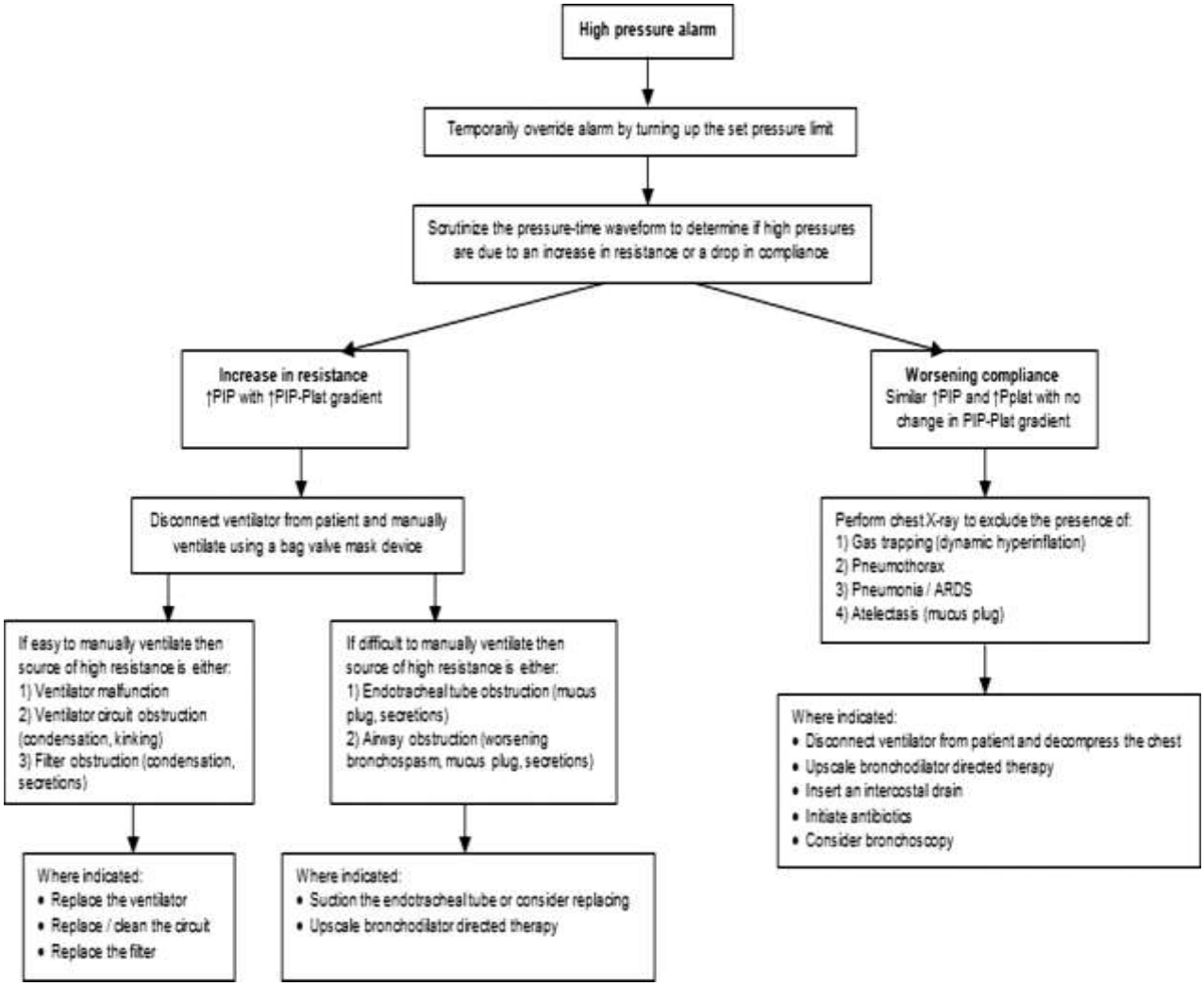

Figure 8: Troubleshooting high ventilator pressures in patients with asthma [26]

Management

When suspecting bronchospasm [5,27]

1. Call for help
2. Switch to 100% Oxygen
3. Stop the stimulation and ventilate by hand
4. Consider anaphylaxis as a differential diagnosis, stop administering suspicious drugs
5. Deepen the level of anaesthesia
6. Check if the tube is not blocked, exclude endobronchial intubation
7. Rule out malfunction of equipment (ventilator/circuit), check the filter for obstruction

Pharmacological treatment

8. First line:
   Salbutamol- 6-8 puffs repeated as necessary (Metered dose inhaler)

9. 2nd line:
   Ipratropium bromide- 0,5mg nebulized 6 hourly
   Mgso4- 50 mg/kg, IV max 2g over 20 min
   Hydrocortisone 200mg 6 hourly
   Ketamine- Bolus 10-20 mcg
   In extremis:
   Adrenaline
   Nebulize – 1:1000

POST- OPERATIVE CARE

The intraoperative course is the one that will determine which post- operative care the patient requires. If the procedure was uneventful; the patient can be taken back to an ordinary ward for post -operative care. It is important to ensure that the asthmatic patient has good pain control and without nausea nor vomiting. [3,5,10,11]
Patients that experienced severe bronchospasm intraoperatively may require postoperative high care or ICU placement; for ventilation so to allow time for airway function recovery and further medical management [5,10].

CONCLUSION

According to the world health organization, the prevalence of asthma is continuing to grow, and anesthetists will come into contact with asthmatic patients more frequently as a result. It is important to know how to manage these patients appropriately and have knowledge on what to do should complications occur. Well controlled asthmatic patients tolerate surgery and anaesthesia very well, however are still at high risk for morbidity and mortality should they get intraoperative bronchospasm.

High risk patients are usually the ones that are poorly controlled, and the group to be undergoing major surgery. As a result, these patients are then at high risk for post operative pulmonary complications. Planning management for these patients during the perioperative assessment is important, and so to get the best clinical outcomes.

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