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Monitoring, Sedation, and Anesthesia for Flexible Fiberoptic Bronchoscopy

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1. Introduction

Since the advent of flexible fiberoptic bronchoscopy (FFB) in the 1970's, the use of sedation and topical anesthesia has allowed the practice of bronchoscopy, specifically FFB, to evolve from the operating room to the outpatient setting. Early techniques of general anesthesia and regional blockade of nerves innervating the airway have been largely replaced by improved techniques of patient monitoring, intravenous conscious sedation, and application of topical anesthetics in the airway. Today the bronchoscopist, in addition to basic FFB techniques such as bronchoalveolar lavage and transbronchial biopsy, can also perform complicated procedures such as removal of foreign bodies, ablation of airway tumors, and endobronchial stenting, all in the outpatient bronchoscopy suite. A continued emphasis has been placed on improvements in patient safety due to the complexities of the procedure itself, but also the role of conscious sedation and topical anesthetics to ensure maximal performance by the bronchoscopist to achieve the desired goal of successful biopsy or other interventions while the patient remains comfortable throughout the entire procedure. A full understanding of the patient's medical history, underlying risk factors such as cardiovascular and pulmonary disease, and medication use is required to plan the requirements for the FFB.

1.1 Guidelines for bronchoscopy

There is some expert consensus guidance published on the use of sedation and topical anesthesia during FFB. The National Institutes of Health published a workshop summary on the investigational use of FFB in patients with asthma in 1985 (National Institutes of Health [NIH], 1985). Further recommendations for investigational FFB in asthmatics was provided in 1991 and commented on potential hazards, high risk and unsuitable patients, and

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procedural limitations (NIH, 1991). The American Thoracic Society (ATS) published a concise one-page guideline in 1987 which outlined diagnostic and therapeutic uses, research applications, conditions with increased risk, and contraindications for FFB (American Thoracic Society [ATS], 1987). It did not, however, provide any specific guidance on the optimal use of topical anesthesia or intravenous sedation. In 2001, the British Thoracic Society published a more complete guideline and made several major recommendations related to sedation and topical anesthesia for all patients undergoing FFB (British Thoracic Society [BTS], 2001). All of the following recommendations had level B evidence (except for #8 with level C) to support their use.

1. Sedation should be offered to patients where there is no contraindication.
2. Atropine is not required routinely before bronchoscopy.
3. Patients should be monitored by pulse oximetry.
4. Oxygen supplementation should be used to achieve an oxygen saturation of at least 90% to reduce the risk of significant arrhythmias during the procedure and also in the postoperative recovery period.
5. The total dose of lidocaine should be limited to 8.2 mg/kg in adults (approximately 29 ml of a 2% solution for a 70 kg patient) with extra care in the elderly or those with liver or cardiac impairment.
6. The minimum amount of lidocaine necessary should be used when instilled through the bronchoscope.
7. Sedatives should be used in incremental doses to achieve adequate sedation and amnesia.
8. Routine ECG monitoring during bronchoscopy is not required but should be considered in those patients with a history of severe cardiac disease and those who have hypoxia despite oxygen supplementation.

A survey of BTS pulmonologists was conducted after the publication of these guidelines (Pickles et al., 2003). A variety of lidocaine (or lignocaine) preparations to include gel, spray, and nebulized were used in 97% of patients with rare use of other anesthetics such as cocaine or amethocaine lozenges. Interestingly, sedation was most commonly done with midazolam but was not used by 27% of respondents citing age, frailty, and medical comorbidities. Assessment of sedation during FFB was most frequently done by measurements of oxygen saturations (98%) and observation of patient response (57%). Similar findings on the lack of standardization were noted in a separate survey of BTS pulmonologists (Smyth et al., 2002).

1.2 Contraindications

The American Thoracic Society (ATS) 1987 guidelines presented four absolute contraindications to the performance of FFB that included: 1) operator inexperience, 2) lack of adequate facilities, 3) absence of informed consent, and 4) inability to maintain adequate oxygenation. Other significant contraindications thought to confer a high risk to patients during FFB included: 1) profound refractory hypoxemia; 2) severe bleeding diathesis uncorrectable prior to the procedure, and 3) malignant cardiac arrhythmias (ATS, 1987). Other medical conditions that also increased the risk of FFB and were listed as relative contraindications included: 1) lack of patient cooperation, 2) recent myocardial infarction or unstable angina, 3) respiratory insufficiency or failure, 4) uremia, 5) unstable asthma, 6)

unstable cardiac arrhythmias, and 7) significant debilitation or malnutrition. The 2001 BTS guidelines do not present any specified contraindications but noted there are no controlled studies of the patient risk factors and each patient must be individually assessed based on the risk-benefit ratio (BTS, 2001).

2. Preparation for bronchoscopy

The goal of patient assessment for any invasive procedure such as FFB is to forewarn of potential complications or to identify complications that occur as a result of the procedure. Possible bronchoscopic complications may include a variety of respiratory, cardiac, and other conditions (Pereira et al., 1978, Suratt et al., 1976). Reported respiratory complications include hypoxia, hypercapnea, laryngospasm, bronchospasm, pulmonary edema, aspiration, airway obstruction, pneumomediastinum and pneumothorax (Facciolongo et al., 2009). Cardiac complications can include vasovagal reactions, tachycardia, bradycardia, dysrhythmias, and myocardial infarction. Other reported complications are airway trauma, hemorrhage, epistaxis, infection, nausea and vomiting, adverse reactions to topical anesthesia, exposure to radiation, and death. In an attempt to avoid these possible events, preparation of the patient begins with the initial assessment and evaluation, and monitoring continues through all phases of FFB.

2.1 Patient evaluation

All patients with an indication for FFB should undergo a historical assessment to identify potential bleeding, respiratory, medication, neurologic, or cardiovascular risks. These could potentially include blood dyscrasias, uremia, anti-coagulant or anti-platelet medications, surgical or dental history, a history of asthma, cervical spine disease, interstitial pneumonia, upper airway obstructions, congenital defects, cardiac history, epilepsy, neoplastic mass or therapies. A previous history of bronchoscopy complications, adverse reactions to sedation, drug or alcohol abuse history may also prove useful (American Society of Anesthesiologists [ASA], 2002). Additionally, a family history for clotting complications or bleeding disorders may suggest when a patient is at higher risk for complication. The airway exam should include an assessment of potential bronchoscope entry points in either nares or mouth for potential risks such as small lumens, excessive deviation, congenital deformities or loose dentition. As some patients require intubation due to procedural complications a Mallampati score, exam of habitus, neck, jaw, and oral structures as they affect direct laryngoscopic intubation are also recommended. Pulmonary exams should include an assessment for tachypnea, increased effort or asymmetry, "barrel-chest", auscultation, cyanosis or clubbing. As bleeding and cardiovascular events have also been reported to complicate bronchoscopy a focused exam to identify potential risk factors in these systems should also be performed. Finally, an American Society of Anesthesiologist's Physical Status Classification should also be recorded (ASA, 2002).

All patients undergoing FFB with sedation should undergo a thorough evaluation to include medical and surgical history, current medications, drug allergies, and amount and type of alcohol and illicit drug use. Medical and surgical history should focus on evaluating the patient's degree of cardiac and respiratory compromise and reserve physiology. Close attention and consideration should be given to those with obstructive lung disease, obstructive sleep apnea, neuromuscular disorders, renal and hepatic impairments. Physical exam should

focus on upper airway abnormalities, assessment of potential difficult airway anatomy, pulmonary system focusing on active airway obstruction, and gross neurologic function.

2.2 Pulmonary function testing

Pulmonary function testing should be performed if there is clinical suspicion for severe obstruction. The BTS guideline suggests testing be performed when forced expiratory volume at one second (FEV₁) is less than 40% predicted or oxygen saturation (SaO₂) is less than 93% (BTS, 2001). One small prospective trial reported a drop of 13.8% in FEV₁ (baseline 1.37 ± 0.16L) approximately 15 minutes into bronchoscopy (Salisbury et al., 1975). A slightly larger retrospective review reported patients who had a FEV₁/forced expiratory volume (FVC) ratio less than 50% or an FEV₁ less than one liter with an FEV₁/FVC ratio less than 69% had a bronchoscopic complication rate of 5% compared to 0.6% of controls with normal spirometric function (Peacock et al., 1994). If the patient requires additional procedures such as bronchoalveolar lavage or transbronchial biopsy and there are concerns for possible respiratory compromise, screening spirometry may also be useful. Lima reported that patients with diffuse lung disease have a decrease of approximately 12.7% in FEV₁ following bronchoalveolar lavage (Lima et al., 2009).

2.3 Radiographic studies

It is assumed that a patient who is scheduled to undergo FFB has already had a chest radiograph performed given the minimal risk and ability to non-invasively assess the thorax. However, if a computed tomography (CT) scan of the chest has not already been performed, it should be considered for patients with hemoptysis or undergoing a neoplastic evaluation. A higher diagnostic sampling yield for malignancy has been reported if the patient had a CT performed prior to bronchoscopy (Bungay et al., 2000; Laroche et al., 2000). Additionally, in cases of hemoptysis, pre-procedural CT was able to improve sampling in patients who were at higher risk for neoplastic associated hemoptysis, obviate the need for invasive evaluation, or help identify areas of bronchiectasis for sampling (McGuinness et al., 1994; Tsoumakidou et al., 2006).

2.4 Laboratory testing

A large number of practitioners empirically order coagulation tests prior to performing FFB. The ability of these tests to predict bleeding risks prior to FFB is controversial and several sources recommend against routine testing (Bjørtuft et al., 1998; Kozak & Brath, 1994; Segal et al., 2005). Additionally, Weiss reported bleeding risks in a group of thrombocytopenic patients with platelet counts less than 100,000 who underwent a total of 58 FFB procedures. There were seven occurrences of epistaxis and/or hemorrhage but only one patient experienced severe epistaxis despite an oral approach and a platelet count of 18,000 (Weiss et al., 1993). Thus, routine testing without significant suspicion for bleeding risk is not recommended. A pre-procedural arterial blood gas is recommended in the 2001 BTS guidelines for the same patients who may benefit from a pre-procedural PFT, FEV₁ less than 40% predicted or SaO₂ <93% (BTS, 2001). There is scant available data to support this recommendation except for the report by Salisbury in which one patient whose PaO₂ plummeted from 60 mm Hg to 38 mm Hg intra-procedurally and resolved with removal of the bronchoscope (Salisbury et al., 1975).

2.5 Anti-platelet medications and anticoagulants

Anti-platelet agents and non-steroidal anti-inflammatory (NSAID) medications are commonly used by patients who have an indication for FFB. While there is a potential for bleeding complications from biopsy, there are few reported cases of complications related to NSAID medication use. Aspirin is not reported to increase the rate of bleeding bronchoscopic complications when compared to controls (Herth et al., 2002). However, the continued use of clopidogrel prior to bronchoscopy has been associated with a bleeding rate of 89% and up to 100% of patients who continued to take both aspirin and clopidogrel together (Ernst et al., 2006). In patients who can tolerate the cessation of antiplatelet therapy, the 2008 American College of Chest Physicians (ACCP) clinical practice guidelines recommend stopping clopidogrel seven to ten days before FFB while Ernst, et al. recommended stopping five to seven days before FFB.(Douketis et al., 2008; Ernst et al., 2006) While the ACCP additionally recommends that NSAID medications be stopped five half-lives prior to a planned procedure with bleeding risk, there is no specific data on FFB to support this statement. Direct thrombin inhibitors and vitamin K antagonists such as warfarin are also commonly used by patients who require bronchoscopy. The 2008 ACCP Clinical Practice guidelines recommend cessation of warfarin for at least five days prior to a procedure with an INR assessment 1-2 days before the procedure for an INR < 1.5. Certain patients, i.e. those with mechanical valves, may also require bridging on other anticoagulants (Douketis et al., 2008).

3. Monitoring during bronchoscopy

3.1 Pre-procedure assessment

Immediately prior to FFB, the patient should be re-evaluated for recent medical events or other changes in condition such as infection or flare of respiratory disease (ASA, 2002; BTS, 2001). Patients who have experienced a recent myocardial infarction are recommended to have the procedure delayed for up to 6 weeks (BTS, 2001). The patient history of oral intake should be confirmed. In healthy patients without modifiers such as delayed gastric emptying, the ASA Pre-Procedure Fasting Guidelines recommend fasting for two hours for clear liquids, four hours for breast milk, and six hours for formula or light meals to decrease the risk of aspiration (ASA, 2002) The BTS guidelines for FFB lower the time limit for light meals to four hours (BTS, 2001). In all patients, intravenous access should be obtained and maintained throughout the procedure. Routine vital signs to confirm systemic and hemodynamic stability are recommended. If the patient has a high risk for cardiovascular disease, consideration should be given to obtain a 12-lead electrocardiogram (Shrader & Lakshminarayan, 1978).

3.2 Intraprocedural monitoring

For patients who will receive a moderate level of sedation (able to maintain spontaneous ventilation and respond to verbal or tactile stimuli), continuous hemodynamic monitoring should be used at five minute intervals (ASA, 2002). While it is uncertain that all patients undergoing FFB would benefit from intra-procedural continuous electrocardiographic monitoring, both societies recommend continued monitoring in patients who are at high cardiovascular risk. (ASA, 2002; BTS, 2001) A study of continuous electrocardiographic

monitoring demonstrated evidence of myocardial ischemia in 17% of 29 patients above the age of 50 undergoing FFB (Matot et al., 1997).

3.3 Supplemental oxygen

The routine use of supplemental oxygen during FFB has previously been a point of disagreement with some authors. Given the known risks for cardiac arrhythmia during periods of hypoxia, both supplemental oxygen administration and monitoring with pulse oximetry are recommended for all patients. The sensitivity of pulse oximetry to detect hypoxia compared to clinical exam should make this a routine part of FFB even in healthy or research patients, especially with the use of conscious sedation (ASA, 2002; BTS, 2001; Shrader & Lakshminarayan, 1978). Ghio et al. demonstrated evidence of hypoxia in healthy volunteers during the initiation of bronchoalveolar lavage (Ghio et al., 2007). Nearly 25% of patients in a study of 1,051 FFB required the use of supplemental oxygen for desaturations (Jones & O'Driscoll, 2000). The BTS recommends using supplemental oxygen to maintain a goal of SaO₂ greater than 89% during and after FFB (BTS, 2001). Patients who undergo FFB are frequently at increased risk for hypercapnea due to intravenous sedation or underlying lung disease (Salisbury et al., 1975). While capnography is also more sensitive to hypercapnea than physical exam, there is no clear recommendation or evidence to support the routine use of capnography during FFB with moderate levels of sedation.

3.4 Post-procedure assessment

After FFB is completed, patients should continue to receive oximetry and be monitored until they are near their baseline state of consciousness and interaction (ASA, 2002). Supplemental oxygen should also be continued until the patient can spontaneously maintain a SaO₂ greater than 89%. The return of the gag reflex and the ability to safely swallow clear liquids should be confirmed (BTS, 2001). If the patient has received transbronchial biopsies with or without fluoroscopic guidance, a chest radiograph should be performed one hour following the procedure (BTS, 2001). Transthoracic ultrasound has recently come to prominence for the ability to identify the presence of pneumothorax, but its routine use following FFB is not yet well established.

4. Sedation

Persons undergoing FFB can experience significant degree of anxiety, sense of asphyxiation, and severe coughing. Sedative and analgesic agents are frequently administered to patients undergoing bronchoscopy to reduce these noxious sensations. Both the ATS and the BTS guidelines recommend the use of sedation during bronchoscopy (ATS, 1987; BTS, 2001). Despite this, debate has continued regarding the necessity of sedation during FFB. Surveys have revealed increased physician comfort and use of sedation during bronchoscopy (McLean et al., 1998; Prakash et al., 1991). Patient satisfaction and willingness to pursue repeat FFB procedures if required has been shown to be higher in those receiving sedative and systemic analgesic agents (Gonzales et al., 2003; Hirose et al., 2008; Putinati et al., 1999; Steinfert & Irvin, 2010). Tolerance to FFB was clearly decreased in a prospective study of 357 patients who received no sedation for their procedure (Lopez et al., 2006). Putinati et al. also demonstrated improved procedural success in those receiving sedative agents. Bronchoscopy was aborted prior to completion in six of fifty patients in the placebo group

(Putinati et al., 1999). Interestingly, Hatton et al. described decreased patient satisfaction and willingness to undergo repeat procedure when comparing midazolam to placebo (Hatton et al., 1994). Subsequent editorial comments highlight the difficulty in evaluating these studies as the results were criticized for insufficient medication dosing and administration sequence (Hanley, 1995).

Previous reviews reveal wide variation in the practice patterns for sedation use during FFB (Matot & Kramer, 2000; Vincent & Silvestri, 2007). No single regimen has been found to be superior and previous guidelines did not have recommended regimens (BTS, 2001). Recently, the American College of Chest Physicians released a consensus statement on topical anesthesia, analgesia and sedation during FFB. The consensus statement suggested the use of lidocaine for topical anesthesia and the combination of a benzodiazepine and opiate administration for sedation and analgesia during the procedure, with propofol as an effective alternative agent (Wahidi et al., 2011). Multiple factors must be taken into consideration when selecting an analgesic and sedative regimen. Patient characteristics include age, co-morbidities, and baseline respiratory physiology. The procedure complexity and time required must be considered as an airway survey and bronchoalveolar lavage invariably requires less time and sedation than more complex procedures such as transbronchial biopsies, mediastinal lymph node sampling, debulking and stenting of endobronchial lesions. The degree of sedation required can vary greatly from mild sedation to general anesthesia (ASA, 2002). Increasingly complex FFB procedures are being performed without the assistance of general anesthesia including mediastinal lymph node staging with endobronchial ultrasound guidance with good patient satisfaction (Steinfort & Irvin, 2010). Finally one must be familiar with the degree of support staff able to provide pre and post-procedural care and monitoring during the recovery process.

4.1 Degree of sedation

The desired degree of sedation and analgesia should be determined for individual patients and follow American Society of Anesthesiologists (ASA) definitions:

1. Minimal Sedation (Anxiolysis): A drug induced state with normal response to verbal stimulation with unaffected airway, spontaneous ventilation and cardiovascular function
2. Moderate Sedation/Analgesia (Conscious Sedation): A drug induced state with purposeful response to verbal or tactile stimulation, no airway interventions required, maintains adequate spontaneous ventilation, and cardiovascular function typically maintained.
3. Deep Sedation/Analgesia: A drug induced state with purposeful response after repeated or painful stimuli, airway intervention may be required, spontaneous ventilation may be inadequate and cardiovascular function typically maintained.
4. General Anesthesia: A drug induced state in which patients are not arousable even with painful stimulus, airway intervention required, spontaneous ventilation frequently inadequate, and cardiovascular function may be impaired.

The level of sedation required for FFB is typically minimal to moderate depending upon the type of procedure planned and is often performed by a non-anesthesiologist. When greater than moderate sedation is desired, those patients with limited cardiovascular or pulmonary

reserve, or prolonged procedure anticipated, it is recommended the expertise of an anesthesiologist be obtained.

4.2 Sedative and analgesic agents

Favorable agent profiles include relatively rapid onset of action, rapid and predictable recovery, with minimal hemodynamic instability and lack of significant respiratory depression at doses achieving desired level of sedation. For these reasons benzodiazepines, opioids, and more recently propofol have been increasingly used for sedation during FFB (Vincent & Silvestri, 2007). Other intravenous agents to improve patient comfort such as atropine are not currently recommended and limited studies have failed to demonstrate a significant benefit (Hasanoglu et al., 2001; Korteweg et al., 2004; Triller et al., 2004)

4.2.1 Benzodiazepines

Benzodiazepines have sedative-hypnotic, anxiolytic, and amnestic effects by interacting on GABA receptors. Frequently used agents include diazepam, midazolam, lorazepam, and temazepam (Greig et al., 1995; Leite et al., 2008; Vincent & Silvestri, 2007; Watts et al., 2005). Oral use of temazepam and diazepam has been described and appear to offer an appropriate degree of mild sedation/anxiolysis (Matot & Kramer, 2000; Watts et al., 2005). The advent of midazolam, a water soluble, short-acting benzodiazepine able to be given intravenously has made it the primary agent in many bronchoscopy suites. The metabolites of midazolam have minimal subsequent effects. Midazolam can be given via intermittent intravenous doses and tailored to patient responses. Caution should be used when administering to the elderly and those with obstructive airway physiology. Sedation is typically effective for 20-40 minutes. Midazolam can be safely given in 0.5mg to 1mg increments at five minute intervals until desired level of sedation achieved. Another desirable attribute to benzodiazepines is the availability of a reversal agent. The competitive antagonist, flumazenil can rapidly reverse the effects of benzodiazepines. Though not standard practice, a study of 22 patients demonstrated successful reversal FB sedation using flumazenil (Williamson et al., 1997). Flumazenil use is typically reserved for benzodiazepine reversal in those patients experiencing sedation related hypoxia, need for improved airway clearance, or increasing hypercarbia. Flumazenil use should be avoided in those patients on chronic benzodiazepines due to possible seizure provocation.

4.2.2 Opiates

Opiates have both sedative and analgesic properties as well as antitussive effects. Frequently used opiate agents include fentanyl, alfentanil, remifentanil, meperidine and less frequently morphine. Many studies have evaluated opiate agents in combination with other sedatives including benzodiazepines and propofol (Greig et al., 1995; Hwang et al., 2005; Leite et al., 2008; Matot & Kramer, 2000; Vincent & Silvestri, 2007; Yoon et al., 2011). Greig et al. demonstrated that a lone opiate agent in combination with a benzodiazepine resulted in a reduced number of coughs and reduced topical lidocaine dose (Greig et al., 1995). Fentanyl and related agents are desired due to rapid onset of action, high potency, and short duration of action. A study of alfentanil with standard dose topical lidocaine revealed improved composite score of sedative effects and adverse events when compared to lidocaine alone or midazolam combined with topical lidocaine. The propofol combination composite score was

slightly superior to alfentanil combination (Leite et al., 2008). All opiates can produce respiratory depression and this is amplified when given in combination with another sedative agent (Yoon et al., 2011). If severe respiratory depression occurs, reversal of opiate agents can be obtained with naloxone use. Due to potential adverse hemodynamic effects of naloxone and sudden opiate reversal, this should be reserved for those patients with clinically significant respiratory depression.

4.2.3 Propofol

Propofol is an alkyl-phenol sedative-hypnotic agent in a lipid emulsion capable of producing a dose-dependent degree of sedation from conscious sedation to general anesthesia. It has a rapid onset of action (less than two minutes) and rapid recovery (less than 15 minutes) (Matot & Kramer, 2000; Vincent & Silvestri, 2007). When compared to alfentanil and midazolam as well as topical lidocaine, propofol had the lowest composite score indicating the lowest complication index (Leite et al., 2008). Propofol has been demonstrated to have improved patient neuropsychometric recovery with no difference in physician procedural sedation satisfaction when compared to midazolam (Clark et al., 2009). Propofol has also been reported to be a safe option for sedation in pediatric patients (Berkenbosch et al., 2004; Larsen et al., 2009). In a retrospective study, it must be noted however that fifty percent of pediatric patients were classified as having minor complications which included the need for supplemental oxygen, oropharyngeal suctioning or jaw-thrust to improve oxygen saturation (Larsen et al., 2009). Propofol in separate combinations with alfentanil and ketamine has been demonstrated to provide patient controlled sedation via a patient-controlled-analgesia device (Hwang et al., 2005). Fospropofol, a water-soluble prodrug of propofol, has been demonstrated to be a safe agent during FFB in a phase three trial (Silvestri et al., 2009). Mild to moderate hypoxia was noted in 15% of the patients given the described optimal sedative dose. One must be aware of and recognize the typically dose dependent hemodynamic effects (hypotension, decreased cardiac output) as well as the rare development of propofol infusion syndrome.

5. Topical anesthesia

Along with sedation, topical airway anesthesia is an important component of FFB as it provides the patient additional comfort and tolerability that sedation alone will not provide. Local anesthesia of the nares, oropharynx, and hypopharynx allows comfortable passage of the bronchoscope to the upper airway. More importantly, topical anesthesia of the airways beyond the glottis blunts the cough reflex and allows the bronchoscopist to visualize the airways and perform necessary procedures. Selected patients such as healthy volunteers with adequate topical anesthesia can tolerate FFB without the need for intravenous sedation (Ghio et al., 1998). There have been a variety of studies that have explored issues of patient comfort, tolerability of FFB and dosing regimens. While patient comfort is the primary goal, the ability for the bronchoscopist to complete the procedure is likewise paramount.

5.1 Administration

There is significant variation in the administration of topical anesthesia during FFB. The optimal preparation largely depends on the patient, the experience of the technician, and the estimated length of the procedure. A typical airway preparation for FFB in our institution

includes the application of 2% viscous lidocaine for the nasal mucosa, nebulized 4% topical lidocaine for oral inhalation prior to the FFB, and application of 1% topical lidocaine during the procedure for additional upper and lower airway mucosal anesthesia to control coughing. This airway preparation uses approximately 500 mg of topical lidocaine. The amount of 1% lidocaine used is highly variable and physician dependent with approximately 100 mg used for direct application to the vocal cords and carina and additional lidocaine used for lower airway anesthesia to suppress coughing. There are relatively few studies examining the optimal lidocaine dosing for patient comfort and safety during FFB. A study examining various lidocaine amounts (mg/kg) and strengths ranging from 1% to 2% in 96 patients found no differences between the six groups in terms of patient comfort (Mainland et al., 2001). The author recommended use of 1% lidocaine for topical airway anesthesia based on similar amounts of supplemental lidocaine doses and serum lidocaine levels. An earlier 1985 study demonstrated there was no effect on patient comfort scores when a fixed dose of 370 mg of lidocaine was compared with higher lidocaine doses with as needed dosing (mean lidocaine dose=512 mg) (Sutherland et al., 1985). Notably, the airway preparation in the fixed dose group used 1% lidocaine versus 2% in the uncontrolled group. A 2008 prospective study evaluating the equivalence of 1% versus 2% topical lidocaine during FFB demonstrated no difference in cough frequency or as needed doses of lidocaine by the bronchoscopist. The 2% lidocaine group received twice the mg/kg dose as the 1% lidocaine without increasing patient comfort (Hasmoni et al., 2008). Finally, the use of nebulized lidocaine during the FFB preparation is equivocal (Keane & McNicholas, 1992). Several studies have demonstrated less cough and safety when comparing nebulized lidocaine with other preparations (Gove et al., 1985; Graham et al., 1992). However, other studies were unable to demonstrate a benefit for nebulized lidocaine compared with saline placebo in terms of cough perception, patient discomfort, or use of supplemental lidocaine doses (Charalampidou et al., 2006; Stolz et al., 2005).

5.2 Agents

Lidocaine (or lignocaine) is the most commonly used topical anesthetic applied to the airway mucosa during FFB. Other agents that may be used include tetracaine (2%), benzocaine (10-20%), and cocaine (4-10%). Lidocaine is preferred as it is less toxic, more widely available to the bronchoscopist, and shorter acting than cocaine or tetracaine. Lidocaine is metabolized by the liver and may have side effects at serum levels greater than 5 microgram/ml. Benzocaine has duration of action of only five to ten minutes and is not ideal for FFB; its use is limited by potential toxicity due to methemoglobinemia. Tetracaine has a longer duration of action but a very narrow margin of safety and is not advocated for use in FFB. Use of cocaine is limited due to excess sympathetic nervous system activity and possible toxicity and potential for abuse. However, direct comparisons of lidocaine with other preparations such as cocaine have shown equivalence in terms of patient tolerance (Teale et al., 1990).

5.3 Dosing of topical anesthesia

Initial guidelines for lidocaine dosing published by the National Institutes of Health (NIH) in 1985 recommended no more than 400 mg cumulative dose of lidocaine for healthy asthmatics undergoing FFB. This recommendation was primarily based on expert opinion (NIH, 1985). The updated 1991 NIH guidelines for FFB in asthmatics simply stated the

lowest topical anesthetic dose possible should be used (NIH, 1991). When the BTS published general guidelines for topical anesthesia in the routine clinical practice of FFB, their recommendation was based primarily on two recently published studies (BTS, 2001). A study of 48 asthmatics undergoing research FFB demonstrated safety with a mean dose of 8.2 mg/kg of lidocaine as the upper limit of normal (Langmack et al., 2000). Another smaller study by Milman et al. of 16 patients undergoing FFB recommended a maximum dosage of 6-7 mg/kg (Milman et al., 1998).

The current medical literature contains a substantial collection of studies evaluating serum lidocaine levels during FFB. These studies evaluating lidocaine dosing have been done to evaluate a variety of techniques in application of topical anesthesia (Ameer et al., 1989; Amitai et al., 1990; Berger et al., 1989; Boye & Bresden, 1979; Efthimiou et al., 1982; Gjonaj et al., 1997; Gomez et al., 1983; Jones et al., 1982; Karvonen et al., 1976; Korttila et al., 1981; Langmack et al., 2000; Le Lorier et al., 1979; Loukides et al., 2000; Mainland et al., 2001; McBurney et al., 1984; Milman et al., 1998; Patterson et al., 1975; Smith et al., 1985; Sucena et al., 2004; Sutherland et al., 1985). These twenty studies were reviewed by Frey et al. in their study of lidocaine dosing (Frey et al., 2008). This compilation of studies included a total of 457 patients whose mean age was 47.4 ± 23.7 years and the mean total dose of lidocaine was 488 ± 463 mg. The mean lidocaine dose (reported as adjusted for weight) was 9.7 ± 5.0 mg/kg. Only six of these studies gave a lidocaine dose greater than 8.2 mg/kg or total dose greater than 600 mg. None of the studies reported an average peak lidocaine level > 5.0 mg/kg, while only three of the 21 studies reported a maximum lidocaine level > 5.0 mg/kg. This cumulative data of nearly 500 patients did not suggest a trend towards lidocaine toxicity despite higher lidocaine levels than the BTS recommendations (Frey et al., 2008). The Frey study collected measured lidocaine dosing and serum levels for 154 patients with a mean age of 64.7 years undergoing FFB. Mean lidocaine usage was 15.4 ± 4.5 mg/kg (1.17 ± 0.20 gm), mean serum lidocaine level was 1.6 ± 0.7 mg/mL, and mean blood methemoglobin level was $0.7 \pm 0.3\%$. No clinical toxicity was noted and the authors adequately demonstrated the safety of higher doses of topical lidocaine (Frey et al., 2008).

Other studies have also demonstrated the safety of higher doses of lidocaine during FFB (Ameer et al., 1989; Gjonaj et al., 1997; Sucena et al., 2004]. In the earliest study in 1979, 12 FOB patients received an average of 600 mg of topical lidocaine. The maximum lidocaine level was found to be 3.79 µg/ml in a patient with hepatic metastases who only received 420 mg topical lidocaine (LeLorier et al., 1979). A follow-up study in 1982 by Efthimiou et al. of 41 FOB patients used a similar mean lidocaine dose (9.3 ± 0.5 mg/kg); mean peak levels were 2.9 ± 0.5 µg/ml and two patients had a lidocaine level > 5 µg/ml with no complications (Efthimiou et al., 1982). Ameer et al. compared an elderly group of 14 patients (mean age of 67 years) with a young group of five patients (mean age of 42 years). Both groups received total lidocaine doses of nearly 1200 mg without significant toxicity. No difference in mean or peak serum lidocaine was found between groups (Ameer et al., 1989). As part of a study evaluating the effect of lidocaine on endobronchial cultures, Berger et al. studied eight patients who received an average total lidocaine dose greater than 2000 mg. The mean serum level was 2.7 µg/ml and the peak level in one patient was 5.5 µg/ml; no toxicity was reported (Berger et al., 1989). In 1997, Gjonaj et al. evaluated 8 mg/kg vs. 4 mg/kg of nebulized 2% lidocaine in a pediatric population and found no evidence of toxicity. The total lidocaine dose for the high-dose group was 10.13 ± 1.26 mg/kg with mean serum lidocaine levels of 1.17 ± 0.54 µg/ml and peak levels of 2.27 µg/ml [Gjonaj et al.,

1997). The most recent studies by Loukides (mean lidocaine dose of 622 ± 20 mg) and Sucena (mean lidocaine dose of 11.6 ± 3.1 mg/kg) also found no toxicities with these doses (Loukides et al., 2000; Sucena et al., 2004). Notably, five of 30 patients studied by Sucena et al. had serum levels greater than $5 \mu\text{g/ml}$ but no clinical toxicity (Sucena et al., 2004).

5.4 Complications

Serious effects of lidocaine toxicity (seizures, methemoglobinemia, respiratory failure, and cardiac arrhythmias) are reported to begin at serum levels $> 5 \mu\text{g/ml}$ (Fahimi et al., 2007; Rodins et al., 2003; Sutherland et al., 1985; Wu et al., 1993). At lower serum concentrations, milder side effects such as drowsiness, dizziness, euphoria, paresthesias, nausea, and vomiting may occur. Consideration should also be given to allergic reactions due to lidocaine administration (Bose & Colt, 2008). Serum lidocaine clearance can be decreased in the elderly, patients with cardiac or liver disease, and those patients taking certain medications such as beta-blockers, cimetidine, or verapamil (Abernethy et al., 1983, Smith et al., 1985, Thomson et al., 1973). Despite these potential toxicities, there are few reports of significant complications related to topical anesthetic administration. An early survey of nearly 25,000 FFB only noted six patients with complications (respiratory arrest, seizures) related to airway anesthesia and only one patient with methemoglobinemia (Credle et al., 1974). Additional concern was raised about volunteer FFB and the use of topical anesthesia was noted when a 19-year-old healthy volunteer died from lidocaine toxicity after undergoing a research FFB (Day et al., 1998).

Although elevated methemoglobin levels are another potential concern with the use of higher lidocaine doses, there is scant information supporting this as a significant clinical issue. The 1974 bronchoscopy survey only noted symptoms related to methemoglobinemia in a single patient who received tetracaine (Credle et al., 1974). Recently, Karim et al. reported three patients who received topical lidocaine who developed clinical evidence of methemoglobinemia; one patient was undergoing FOB and was taking trimethoprim-sulfamethoxazole (Karim et al., 2011). Most reported methemoglobinemia cases have been in association with benzocaine used in combination with lidocaine or as the sole topical anesthetic (Kern et al., 2000; Kucshner et al., 2000; O'Donohue & Moss, 1980; Rodriguez et al., 1994).

6. Bronchoscopy in the ICU

The 2001 BTS guidelines comment specifically on the differences for FFB performed in the intensive care unit (ICU) (BTS, 2001). There are a significant range of diagnostic (endobronchial cultures, lung collapse, hemoptysis, acute inhalation injury) and therapeutic (excess secretions, treatment of hemoptysis, foreign body removal) indications reported in the ICU setting (Anzueto et al., 1992; Shennib & Baislam, 1996). Intensive care units should be able to provide urgent and timely FFB to carry out these indications. From a safety perspective, these critically ill patients should be considered high risk for complications and absolutely require physiological monitoring during and after the procedure. In ventilated patients, the bronchoscopist can achieve higher levels of sedation and/or anesthesia to complete the diagnostic or therapeutic requirements for FFB. However, the bronchoscope must be able to pass easily through the endotracheal tube and the technique must allow adequate ventilation and oxygenation throughout (BTS, 2001). Hertz et al. demonstrated

that bronchoalveolar lavage could be performed successfully in ventilated patients without complications by using specific bronchoscopy techniques and proper ventilator management (Hertz et al., 1991)

7. Conclusion

Flexible fiberoptic bronchoscopy is a very important and useful tool for the pulmonologist to diagnose and treat various pulmonary disorders. Overall, it is a very safe procedure with low complication rates reported. There are several published guidelines to provide general guidance on the conduct of FFB. With proper preparation of the patient and close monitoring of the patient's condition, FFB can be performed with the desired outcome. An important component of the overall process is to ensure that the patient is both as safe and comfortable as possible. Choosing the proper agent and level of sedation along with adequate topical anesthesia can make the experience better for the patient and the bronchoscopist. This chapter has provided a broad delineation of the studies in the medical literature that address the role of monitoring, oxygen supplementation, intravenous sedation, and topical anesthesia.

8. References

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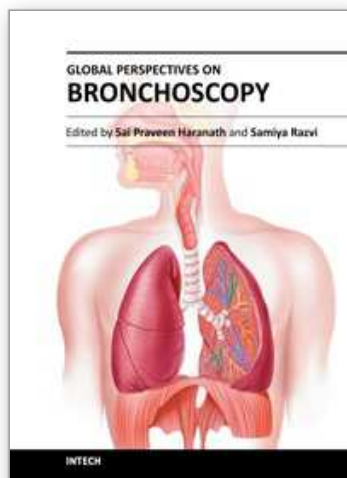
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Bronchoscopy has become an essential part of modern medicine . Recent advances in technology have allowed integration of ultrasound with this tool. The use of lasers along with bronchoscopes has increased the therapeutic utility of this device. Globally an increasing number of pulmonary specialists, anaesthesiologists and thoracic surgeons are using the bronchoscope to expedite diagnosis and treatment. The current volume on bronchoscopy adds to the vast body of knowledge on this topic. The democratic online access to this body of knowledge will greatly increase the ease with which both trainees and expert bronchoscopists can learn more .The contributions from around the world cover the breadth of this field and includes cutting edge uses as well as a section on pediatric bronchoscopy . The book has been an effort by excellent authors and editors and will surely be a often reviewed addition to your digital bookshelf. . In summary, this book is a great testament to the power of collaboration and is a superb resource for doctors in training, ancillary team members as well as practicing healthcare providers who have to perform or arrange for bronchoscopy or the associated procedures.

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