

Preparing of the Patient, Performing Diagnostic Flexible Bronchoscopy and Sampling from the Airways

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Monaldi Arch Chest Dis 2011; 75: 1, 32-38.

Keywords: *Bronchoscopy, Anaesthesia, Sedation, Central lesions, Sampling techniques.*

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Preparing the patient

The preparation of the patient is a crucial time as it can contribute to the success of the bronchoscopic examination. First and foremost, preparation provides the patient with correct information regarding the procedure by which bronchoscopy is performed and informs him/her of sensations that may be felt. The anxiety and worry manifested by the majority of patients undergoing bronchoscopic examination can in a large part be alleviated by the behaviour of the operators, who must reassure the patient and put them at ease [1] (*Level of evidence: III*).

Bronchoscopy is carried out with the patient fasting, in order to reduce the volume and acidity of the stomach contents, thus avoiding the risk of possible regurgitation and aspiration of gastric material. A minimum of eight hours' fasting before the bronchoscopy is carried out is recommended [2] (*Level of evidence: IV*). The Guidelines of the British Society recommend four hours' fasting [3]. It does not in fact appear that a relatively long fasting time is associated with a lower risk of regurgitation. A meta-analysis [4] of 38 randomised controlled studies on different protocols for pre-operative preparation and post-operative complications found that there is no evidence that a reduction in fasting times, with liquids being taken, is associated with a greater risk of aspiration-regurgitation (*Level of evidence: Ia*). Drugs for chronic disorders (e.g. anti-hypertensive drugs, digitalis) can therefore be taken normally, with a very small quantity of water.

Premedication

The rationale for premedication with anticholinergics (atropine, glycopyrrolate) is based on the anti-sialagogue effect which these drugs have, i.e. the inhibition of the vasovagal reflexes (anti-bradycardia activity) and of bronchoconstriction. No real usefulness however has been demonstrated for their routine use, to offset their potential

risks (tachyarrhythmia, acute glaucoma, water retention) (*Level of evidence: Ib*). In a randomised double-blinded study [5], 217 patients undergoing bronchoscopy with sedation (midazolam) were examined, assigned respectively to the atropine (0.01 mg/kg), glycopyrrolate (0.005 mg/kg) and placebo groups. No significant difference was observed in the two pre-medicated groups compared with the control group as regards the control of secretions, the amount of anaesthetic used, the incidence of complications or tolerance of the procedure. Similar results were reported in another study [6] in which 55 randomised patients (25 pre-medicated with atropine and 30 in the control group) underwent bronchoscopy with Holter-ECG monitoring for 24 hours starting from the beginning of the examination, and no significant difference was found between the two groups as regards the onset of arrhythmias or bradycardia. In addition, no difference was observed between the two groups as regards the extent and control of bronchial secretions (*Level of evidence: Ib*).

Sedation

Although the routine use of sedation is not still considered a prerequisite for performing a bronchoscopy, the literature suggests its use [7]. The rationale for sedation is to reduce the state of anxiety, to induce a degree of amnesia but at the same time to keep the patient conscious, capable of collaborating, breathing spontaneously and with adequate ventilation and oxygenation.

Good tolerance of the bronchoscopy on the part of the patient translates into greater facility for the endoscopist in performing the procedure; in addition, the degree of amnesia induced by the sedation makes it easier to perform any subsequent bronchoscopy [8]. The effects of the administration of propofol was evaluated in 18 patients subjected to bronchoscopy under local anaesthesia, observing better tolerance of the examination in the sedated group, while in the control group, be-

sides greater discomfort, an increase was reported in cardiac frequency and systemic arterial pressure [9]. No significant differences, however, were observed regarding the reduction of oxy-haemoglobin saturation during the examination (*Level of evidence: Ib*). In another study [10] the cardiovascular effects consequent on sedation with propofol and midazolam in 100 patients undergoing bronchoscopy were compared, and better control of pressure values and cardiac frequency in the group sedated with propofol was observed, also reporting good tolerance by patients with pre-existing pulmonary disease (*Level of evidence: Ib*). Good results were obtained with the use of benzodiazepine. A randomised study [11] on 100 patients undergoing bronchoscopy, proved better tolerance in patients treated with diazepam compared with those not treated, without significant cardiovascular changes (episodes of desaturation did not differ significantly between the two groups) (*Level of evidence: Ib*). Midazolam (soluble benzodiazepine) is one of the most widely-used drugs because of the manageability it provides in relation to the brief duration of its action (two hour half-life) and its good sedative and amnesic action. Satisfactory sedation is obtained at a dosage of 2.5 mg in the majority of patients [12]. In a survey on performing bronchoscopy in England and Wales, midazolam appeared to be the drug of choice in 85% of cases [13] (*Level of evidence: IV*).

The use of opioids seems to ensure better control of coughing, but it does not affect comfort and tolerance of the examination in terms of reduction of anxiety [14]. The combination of opioids and benzodiazepine has been reported to be effective in controlling coughing, especially when invasive procedures are planned. Good results [15] have been reported with the combination midazolam-hydrocodone (120 randomised patients, subjected to sedation with midazolam and opiate vs midazolam alone). The patients treated with the combination had better control of coughing and better tolerance of the examination compared with the group treated with midazolam alone, without significant changes between the two groups as regards saturation (*Level of evidence: Ib*).

Recommendations

- **The explanatory interview (on how and why the bronchoscopy is being carried out) prepares and reassures the patient in terms of the procedure and facilitates tolerance (Grade C).**
- **A fasting period of 4 hours before the examination is sufficient (Grade B).**
- **The treatment usually given (antihypertensive drugs, etc.) can be taken by mouth with water, even in the four hours preceding the procedure (Grade A).**
- **A peripheral vein must always be cannulated, irrespective of whether sedative drugs are used, in order to**

have a rapid access route in the event that it should become necessary to administer drugs during the course of the procedure or at the end (Grade C).

- **Premedication with atropine does not significantly reduce the risk of cardiac complications and does not offer benefits in the control of secretions. Its routine use is therefore not justified (Grade B).**
- **Sedation improves tolerance of the procedure on the part of the patient (control of anxiety and of the haemodynamic parameters) and facilitates its execution; it should be used except in the case of obvious contraindications (Grade B).**

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Local anaesthesia

Lidocaine is the most widely-used substance as a topical anaesthetic in the respiratory tree and is available in aqueous solution (1, 2 or 4%), gel (4%), unguent (5%), and metered spray (10%, 10 mg per spray). The duration of the action is about 15-20 minutes, and absorption is slower in the upper respiratory tracts (nose, pharynx, larynx) compared with the tracheobronchial tree (which has a larger surface area). Plasmatic concentration is consequently greater when instilled into the lower airways. Since lidocaine is metabolised in the liver, it must be administered with caution in patients with liver diseases and used carefully in patients with low cardiac ejection (depression of myocardial contractility and arrest) [1, 2]. In a study [3] the seric concentration of lidocaine was measured in 16 patients undergoing bronchoscopy, without evidence of adverse effects within a dosage of 500 mg (*Level of evidence: IIa*). In a randomised study [4] carried out on 96 patients undergoing bronchoscopy, equal efficacy (control of coughing, tolerance of the examination and need for further administration during the examination) was encountered in the use of lidocaine at 1% and at 2%, no adverse effect being observed for a maximum plasmatic concentration of 5.02 and 6.28 mcg/ml (*Level of evidence: Ib*). In a study carried out on 51 asthmatic patients subjected to bronchoscopy [5], toxicity was not observed for a maximum lidocaine dosage of 600 mg, equivalent to 8.2 mg/kg (*Level of evidence: IIa*). In patients with liver or cardiac diseases a recommendation was made not to exceed a dose of 5 mg/kg [6, 7]. Administration methods include nebulisation, instillation through the bronchoscope and transcricoidal injection (the latter is currently rarely used as it is less comfortable than the other methods). It has been demonstrated [8] that administration of lidocaine by nebulisation before bronchoscopy reduces the necessity for further administration by the endobronchial route, lowering the risk of toxicity (the plasmatic level is dose-dependent) (*Level of evidence: IIa*). Different conclusions were however drawn by another prospective randomised study [9], in which the average dosage of lidocaine was higher in the group of patients subjected to pre-examination nebulisation than in the placebo group, demonstrating furthermore that nebulisation had no effect in the reduction of coughing or in improving tolerance of the examination (*Level of evidence: Ib*).

The use of lidocaine in gel form seems better than the spray formulation in topical anaesthesia of the nose. The spray formulation and gel were compared [10], and a lower degree of pain was reported in the group of patients anaesthetised with gel (*Level of evidence: Ib*). Similar conclusions were drawn when evaluating three different methods of topical nasal anaesthesia (gel, spray and tampons moistened with lidocaine in solution), and it was reported that the use of gel was the least irritating procedure and the one preferred by patients [11] (*Level of evidence: Ib*).

Recommendations

- **The maximum dose of lidocaine in the execution of a bronchoscopy should be limited to 8.2 mg/kg of bodyweight, with the total dosage anyway not exceeding 600 mg (Grade B).**
- **In patients with liver or cardiac diseases the dosage should not exceed 5 mg/kg of body-weight (Grade B).**
- **Nebulisation of lidocaine does not improve tolerance of the examination nor reduce the total dose of anaesthetic used (Grade A).**
- **Lidocaine in a gel preparation is preferable for nasal anaesthesia (Grade A).**

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Performing fiberoptic bronchoscopy

Fiberoptic bronchoscopy is a procedure carried out under local anaesthetic with the patient seated or lying down. The choice of position for the patient and for the performance of the examination (from the front or from behind) depend on the operator's habitual practice; if the examination is performed with the patient seated, a chair must be

used which is readily reclinable if the necessity arises. The bronchoscope may be introduced nasally, orally or by tracheostomy.

The choice of the nasal or oral route depends also on the experience of the operator [1, 2]. Some authors suggest the nasal route because it offers a more direct anatomical path (which is preferable when positioning a tracheal tube), a more stable position for the instrument (useful in the case of transbronchial needle aspiration, use of lasers or argon plasma coagulation), and better control of secretions from the oral cavity. Conversely, the oral route is preferable in the case of congenital or post-surgical anomalies, removal of foreign bodies and in the case of severe disorders of the coagulation with haemorrhagic diathesis (possible nosebleeds). There are no studies which recommend the choice of one route rather than the other (*Level of evidence: IV*).

Recommendations

- **Fibre-optic bronchoscopy can be carried out either with the patient seated or with the patient supine. In the event that the examination is being performed with the patient seated, it is necessary to use a chair which is readily reclinable (Grade C).**
- **Use of the nasal route is preferable when carrying out bronchoscopy; the oral route should be reserved for cases of occlusion or restriction of the nasal cavities, in the event of disturbances to coagulation or when there is a suspected foreign body (Grade C).**

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Administration of oxygen

The appearance of hypoxemia is a fairly frequent phenomenon in the course of a bronchoscopy and may persist for some hours after the procedure. The causes which induce a reduction in partial oxygen pressure (PaO_2) include excessive sedation, suction manoeuvres which remove oxygen and reduce pulmonary volumes below the residual functional capacity, bronchospasm, and alveolar collapse caused by bleeding or by instillation of fluids [1, 2]. Hypoxemia can give rise to arrhythmias and it is therefore important to maintain during the examination a degree of saturation which allows the examination to be carried out without incurring this risk. An oxy-haemoglobin

saturation value of 90% has been indicated as a minimum level for carrying out a bronchoscopy in safety, with constant monitoring of the patient by pulse oxymeter. In a randomised study on 160 patients subjected to bronchoscopy [3], the patients were divided into four groups of which the first had no oxygen administered, and the others were administered respectively 2 l/min by nasal prongs, 2 l/min by pharyngeal catheter and 3 l/min by pharyngeal catheter. Group 1 (without oxygen) manifested oxy-haemoglobin saturation of 85% with incidence of tachycardia and bradycardia in 20% of cases, while group 4 (oxygen at 3 l/min) maintained a saturation of 94% with tachycardia and bradycardia in 10% of cases. The administration of oxygen reduced the incidence of arrhythmias by 50% (*Level of evidence Ib*). Discordant opinions are reported in the literature as regards the routine administration of oxygen during bronchoscopy (in patients who present a basal saturation level above 90%). In 1,051 patients subjected to bronchoscopy without supplemental administration of oxygen before the procedure and with known FEV_1 [4], administration of oxygen became necessary during or at the end of the procedure in only 151 patients (14%), while 101 patients (9.6%) had transient desaturation without the need for correction with oxygen. A significant correlation was furthermore observed between FEV_1 value and desaturation (the lower FEV_1 value, the greater was the need for oxygen), while sedation (midazolam) did not influence the probability of the occurrence of desaturation. In this study supplemental oxygen was administered in 35% of patients with FEV_1 below 1 litre, in 14% of patients with FEV_1 of 1-1.5 l, and only in 7% of cases with FEV_1 above 1.5 l. On the basis of these results, the authors concluded that desaturation can occur in the course of bronchoscopy for any value of FEV_1 and irrespective of the sedation used, but the majority of patients do not require the administration of oxygen, especially those who have an FEV_1 greater than 1.5 l (*Level of evidence: III*). Similar results but different considerations were reported in another study on 44 patients [5] who did not include anyone with a PaO_2 below 65 mmHg, known cardiovascular illnesses or risk factors for cardiovascular disease. It was observed that many patients showed desaturation independently of the use of sedation and with normal PaO_2 values before the bronchoscopy. The most important factor which correlates with desaturation is the presence of an obstructive component, but since FEV_1 is not capable of predicting the possibility of the appearance of desaturation, and since desaturation can appear for any value of FEV_1 even in patients with normal arterial saturation of oxygen, the administration of oxygen should be carried out routinely during bronchoscopy (*Level of evidence: IV*). Patients considered at risk for hypoxemia in the course of bronchoscopy are elderly subjects (>80) with pulmonary fibrosis. In a study on 336 elderly patients subjected to bronchoscopy [7], an incidence of desaturation of 55% was observed in patients with fibrosis, but only in 16% of cases the administration

of oxygen was necessary (*Level of evidence: III*). In a randomised study on 97 patients subjected to bronchoscopy there were no significant differences in terms of SaO₂ between delivering oxygen with nasal prongs and by cannula through the mouth (*Level of evidence: Ib*). In a randomised study conducted on 34 patients subjected to bronchoscopy with sedation (diazepam), patients with altered pulmonary function in whom the oxygen was suspended immediately after the procedure had episodes of desaturation not pointed out in the group in which oxygen was maintained for the two subsequent hours. The authors suggest maintaining the administration of oxygen for two hours in sedated patients and in those with functional alterations (FEV₁<75% of predicted value), until the initial values are recovered [8] (*Level of evidence: Ib*).

Recommendations

- **All patients must be monitored by pulse oxymeter during bronchoscopy (Grade B).**
- **The pulse oxymeter must be positioned before the administration of sedatives (Grade C).**
- **The administration of oxygen during bronchoscopy is obligatory in patients with basal SaO₂ lower than 90%, in cases of desaturation (<90%) and in patients with cardiac diseases (risk of arrhythmia) (Grade B).**
- **In patients with basal saturation levels >90% the administration of oxygen is not recommended as routine (Grade B).**
- **The administration of oxygen must be kept up with monitoring by pulse oxymeter for 1-2 hours after the end of the bronchoscopy in patients with cardiac diseases, in those with altered pulmonary function, and in the event that profound sedation becomes necessary (Grade B).**

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Bronchial washing, brushing, bronchial biopsy

The principal sampling methods used to take samples of endoscopically visible bronchial lesions are bronchial washing, brushing and biopsy.

Bronchial washing is a simple sampling technique and consists of instilling 20 ml of sterile saline solution into the bronchial tree, which is recovered and sent to the laboratory for cytological, immunological and microbiological tests. Brushing is a cytological sampling technique in which special small brushes are introduced into the working channel of the bronchoscope; the material retrieved is smeared on a glass slide and fixed in ethyl alcohol. Single-use brushes are preferable to the reusable type, diagnostic yield being equal, because of the risk of possible contamination and cross-infection [1]. Bronchial biopsy provides histology tissue specimens, but the material sampled can also be used for a cytological analysis, thus increasing the diagnostic yield, smearing the tissue fragment on glass [2] or immersing the biopsy fragments in rinse solution before transferring them to formalin [3].

The number of biopsy samples reported in the literature as necessary for a good diagnostic yield in lung cancer varies from three to six in central lesions [4, 5]. A study on 271 patients, of whom 215 had endoscopically visible tumours [4] demonstrated a diagnostic yield of 65.2% with a single biopsy sample, while five biopsies were necessary for reaching a sensitivity of 90% (*Level of evidence: III*). The BTS guidelines recommend five biopsy samples where there is a suspicion of neoplastic lesion [6].

There are many reports in literature concerning the use and sensitivity of the three sampling methods, both evaluated individually and in combination, in the diagnosis of lung cancer. Sensitivity is reported [7] for bronchial washing, brushing and biopsy in central lesions of 27-90%, 44-94% and 51-97% respectively, while in peripheral lesions the sensitivity of brushing is 48%, and that of bronchial washing much lower at 28%. Brushing provides a better diagnostic yield in cases of infiltrative lesions, while biopsy, which has good sensitivity in vegetative lesions, shows a lower diagnostic yield in the infiltrative forms and in those with a large necrotic component.

In a meta-analytic study [8] concerning the sensitivity of the various sampling techniques in suspected neoplastic lesions, the best yield in central lesions is given by bronchial biopsy (74%),

then by brushing (59%) and by bronchial washing (43%); overall sensitivity of the three methods combined is 88% (*Level of evidence: IIa*).

In a study conducted on 98 patients with central lesion [9], a sensitivity of 82% is reported for biopsy, 68.4% for brushing and 31.6% for bronchial washing. The combined use of biopsy and brushing increases sensitivity for malignancy to 88%, while no increase in sensitivity is found with the combination of bronchial biopsy and bronchial washing. A low diagnostic yield is reported for bronchial washing (22.7%) in peripheral neoplastic lesions [10]. In 56 patients affected by central neoplastic lesions and subjected to biopsy, brushing and washing, the sensitivity of the methods was respectively 95.5%, 79.5% and 56.8%. Brushing was the sole diagnostic means in 4.5% of the cases, while in no cases did bronchial washing alone allow diagnosis [11]. Similar results are reported in another study [12], which demonstrates a minimal alteration in sensitivity for malignancy in central lesions when biopsy (85.3%) is combined with washing and brushing (88.1%). In a retrospective analysis [13], bronchial washing was the sole diagnostic procedure in central neoplastic lesions in 6 out of 222 patients (2.7%), with a greater sensitivity in lesions with a necrotic component, and low probability of diagnostic yield in bleeding lesions. The use of bronchial washing in addition to biopsy and brushing in central lesions does not have an acceptable cost/efficacy ratio, and its use may find a rationale only in selected cases, such as neoplastic lesions with a large necrotic component or in case of negativity of biopsies and brushing. The combined use of biopsy and brushing was considered [14] the best combination in the diagnosis of central neoplastic lesions (sensitivity 78%), while washing has an extremely low diagnostic yield. An evaluation was performed recently of the role of bronchial washing carried out before and after biopsy and brushing, in terms of diagnostic yield and cost, in patients with suspected lung cancer [15]. The global diagnostic yield was 76% and 36% respectively for central and peripheral lesions when washing was carried out before biopsy and brushing, and 74% and 42% when washing was carried out after biopsy and brushing. In 6% of cases washing was the only component which allowed the diagnosis of malignancy. No significant differences were demonstrated in the diagnostic yield of washing carried out before and after sampling with forceps or brush. The authors conclude that although the additional diagnostic yield offered by washing and by brushing is relatively low, the cost/benefit ratio justifies their use in patients with suspected lung cancer.

On the basis of these studies it is evident that the best sensitivity in central lesions is obtained with biopsy forceps (*Level of evidence: III*), and that the combination of biopsy and brushing increases the diagnostic yield significantly (*Level of evidence: III*). Bronchial washing considered as a stand-alone procedure has a low sensitivity and little impact on altering sensitivity when it is com-

bined with the other sampling methods (*Level of evidence: III*).

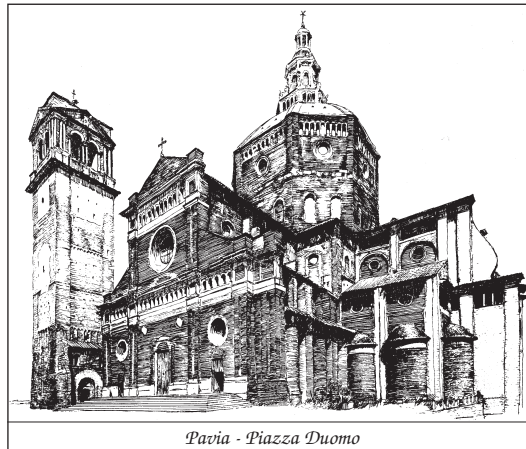
Recommendations

- **In cases of central bronchogenic lesion the biopsy forceps must be considered as the sampling instrument of first choice (Grade B).**
- **In central lesions a minimum of three biopsy samples are required for a good diagnostic yield (Grade B); five samples are recommended for a high probability of diagnosis of malignancy (Grade B).**
- **The combination of bronchial biopsy and brushing can be used to increase the diagnostic yield in central lesions, especially in case of an infiltrative pattern (Grade B).**
- **The routine use of bronchial washing is not justified, considered as a single procedure or in combination, in the diagnosis of central lesions (Grade B).**

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Pavia - Piazza Duomo