Total intravenous anaesthesia- Target Controlled Infusion and Superimposed High-Frequency Jet Ventilation – an anaesthetic protocol for interventional bronchoscopy in cancer patients

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Abstract

Introduction: Diagnostic or therapeutic bronchoscopy may be performed under general anaesthesia in special circumstances aiming for patient safety and operator comfort. Tracheobronchial instrumentation requires an open system ventilatory support. We report the first case series of oncologic patients managed with Total Intravenous Anaesthesia–Target Controlled Infusion (TIVA-TCI) and Superimposed High-Frequency Jet Ventilation (SHFJV) during flexible and rigid bronchoscopy in our institution. We evaluated the safety profile of this technique in cancer patients. Methods: We analysed 24 oncological patients requiring bronchoscopy under general anaesthesia during a 9 months period. The anaesthetic protocol consisted in TIVA-TCI with propofol, Schnider model, site effect concentration, with standard intra-anaesthetic monitoring plus hypnosis and neuromuscular function monitoring and SHFJV using Twin Stream™ ventilator. Results: A number of 25 interventions were performed - 19 flexible and 6 rigid bronchoscopy. During the procedures, optimal anaesthesia depth (bispectral index=40-60) was maintained with a mean propofol site effect concentration Ce=3.1 (+/-0.6) µg/ml. Hemodynamic parameters varied +/-10-20% of preoperative values. SpO_2 was stable with a mean value of 98.5% (FiO_2=0.5-1) and intermittently measured $etCO_2$ had a mean value of 32 (+/-5.4) mmHg. Airway pressures varied according to procedural particularities with a safety upper limit of 25 mmHg. We recorded no intra-anaesthetic or post-interventional complications. Conclusion: The anaesthetic protocol including TIVA-TCI and SHFJV is a safe and effective method of maintaining adequate depth of anaesthesia, cardiovascular stability and gas exchange during diagnostic or therapeutic bronchoscopy in cancer patients.

Keywords: *superimposed high frequency ventilation, TIVA-TCI, cancer patients, interventional bronchoscopy*.

Introduction

The diagnostic and/or therapeutic tracheobronchial instrumentation consisting of flexible or rigid bronchoscopy can be an unpleasant, painful or technically difficult procedure. In order to ensure patient safety and operator comfort some of these procedures must be performed under general anaesthesia.

Providing an adequate oxygenation and ventilation during these interventions can be sometimes challenging, even in patients with normal lung function, due to the concomitant manipulation of the airway. Historically,

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several methods of ventilation have been used: apneic oxygenation, spontaneous assisted ventilation, controlled ventilation in a closed system, manual jet ventilation and high-frequency jet ventilation (HFJV) [1]. Jet ventilation techniques, defined as the injection of a gas through a small tube using a high pressure gas source (1-3 bar), are now increasingly applied in ENT surgery, pneumology, thoracic surgery and intensive care. Two modes of jet ventilation are currently available. The manual jet ventilation was originally described in 1967 [2] and has the advantage of a low cost equipment. It is now replaced by HFJV, an automated ventilatory support largely used to facilitate airway procedures [3]. In both types of jet ventilation complications as hypercapnia, barotrauma or hypoxia may occur [4, 5].

Superimposed High-Frequency Jet Ventilation (SHFJV) is a newly developed technique consisting in a combination of two jet streams - a pulsatile high-frequency jet ventilation (HF) (50-1500/min) and a lownormal frequency jet ventilation (NF) (12-20/min) that can be separately or simultaneously applied [6]. The ventilation in this open system results from the combination of set driving pressure, frequency and inspiratory/expiratory ratio. The high frequency jet ventilation generates an expiratory plateau pressure creating a positive end expiratory pressure responsible for the oxygenation through diffusion mechanisms. The normal frequency ventilation jet creates an inspiratory plateau pressure which is responsible for the elimination of CO_2 through convection mechanism [7].

Challenges to perform safe general anaesthesia in cancer patients with multiple comorbidities and often marginal pulmonary function include: limited availability of specialized equipment, the need for additional training and lack of experience with uncommon techniques, and the need for rapid onset/offset of the anaesthetic effects.

In the present study we report our initial experience using TIVA-TCI and SHFJV in diagnostic and interventional bronchoscopy in a case series of cancer patients. We analysed the safety profile of this anaesthetic protocol developed for these interventions.

Methods

Patient characteristics

All 24 consecutive patients proposed for flexible/rigid bronchoscopy under general anaesthesia were analysed. Patients were enrolled in the first 9 months of SHFJV use in our institution. The majority of patients had suspected or confirmed lung cancer and they were scheduled for diagnostic or staging bronchoscopy.

Patient characteristics, diagnosis and types of the procedures are listed in Tables 1, 2, 3 respectively.

Table 1. Patient data.

	All patients (n=24)
Age (yr)	58.2 (±10.2)*
Sex ratio M/F	17/7
Weight (kg)	67 (±11)*
Height (cm)	167 (±8.3)*
ASA status (II/III)**	16/8

*mean (±SD), **American Society of Anesthesiologists

Table 2. Diagnosis of patients undergoing bronchoscopy under SHFJV

Diagnosis	Total (n=24)
Lung cancer	19
Hodgkin disease	2
Mediastinal nodes	2
Foreign bodies	1

Table 3. Technique and endoscopic intervention performed under SHFJV

Technique	Intervention	Total (n=25)
Flexible bronchoscopy	EBUS TBNA* diagnosis	19
Rigid bronchoscopy	Tumoral biopsy	3
	Intrabronchial glue instillation for fistula closure	2
	Foreign body extraction	1

*EBUS TBNA - Endobronchial ultrasound-guided transbronchial needle aspiration

Mean duration of general anaesthesia for endoscopic intervention was 68 (+/-16.6) minutes.

The following parameters were recorded in each patient: hemodynamics – heart rate (HR), blood pressure (BP), oxygenation - SpO_2, hypnosis - bispectral index (BIS), ventilation - $etCO_2$, airway pressures and muscle relaxation - TOF ratio. We analysed the recorded data measured before, during (every 5 minute) and after the procedure.

Anaesthetic protocol

We used a standardized general anaesthesia consisting of preoperative assessment, propofol TIVA-TCI, effect site concentration, fentanyl and rocuronium, standard, BIS and TOF monitoring and open system ventilation with SHFJV. The emergence consisted of rocuronium reversal (sugammadex) and interruption of propofol TCI.

Preoperative assessment

Preoperative airway assessment was focused on teeth mobility, interdental distance and neck range of motion. Full blood count, glycaemia, electrolytes, renal function, coagulation tests, chest imaging (CT) and electrocardiogram were performed before the intervention. Contraindications for the procedure were acute respiratory failure, significant arrhythmias, decompensated heart failure and high bleeding risk. All patients followed the European Society of Anesthesiology preoperative fasting protocol [8].

Anaesthetic technique

After three minutes preoxygenation with FiO_2=1, anaesthesia was induced with fentanyl 1-5 µg/kg, lidocaine 1 mg/kg, propofol - TCI, Schnider model, setting a variable site effect concentration (Ce) between 4.0 and 6.0 µg/ml based on BIS values, and rocuronium bromide 0.6 mg/kg. The patients were ventilated using face mask and close circuit untill TOF value reached two twitches, followed by the insertion of rigid bronchoscope or a laryngeal mask in case of flexible bronchoscopy. Anaesthesia was maintained with propofol TCI Ce between 2.5-4 µg/ml, in order to maintain an adequate hypnosis (BIS=40-60). fentanyl 2 µg/kg and rocuronium bromide 0.2 mg/kg were given as required. sugammadex, was used to reverse rocuronium at the end of the procedure. The dose was adjusted to the level of neuromuscular blockade – 2 or 4 mg/kg.

Ventilation technique

Jet ventilation was performed with Twin Stream™ (Carl Reiner GmbH, Vienna, Austria) jet ventilator (Figure 1) containing two separately or simultaneously functioning ventilation units: high frequency (HF) ventilator and normal frequency (NF) ventilator (Figure 2).

Fig. 1. Twin Stream jet ventilator

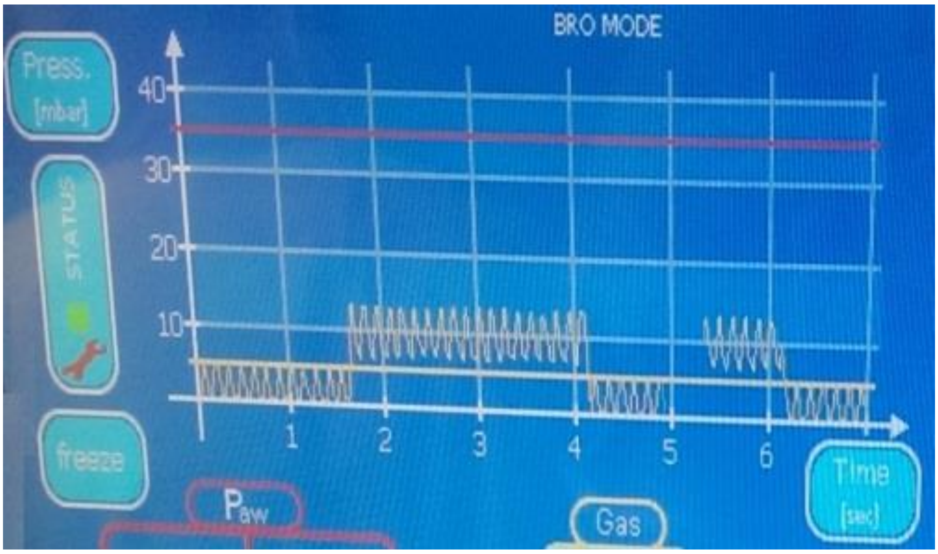

Fig. 2. High frequency and normal frequency jet ventilation

For flexible bronchoscopy procedures – endobronchial ultrasound transbronchial needle aspiration (EBUS TBNA) - a laryngeal mask (LMA) was inserted after the induction of anesthesia. The proper position of LMA was initially checked with closed ventilation circuit. A Jet–Converter (Carl Reiner GmbH, Vienna, Austria) was attached to the LMA for supraglottic jet ventilation (Figure 3). In patients with rigid bronchoscopy trachea was intubated with a Jet-Bronchoscope (Carl Reiner GmbH, Vienna, Austria).

Fig. 3. Jet–Converter attached to the laryngeal mask

Four lumen catheters bronchoscopy (BRO) mode was used in all patients. Two ventilation catheters - HF (green) and NF (white) - and two monitoring catheters - airway pressures (red) - peak inspiratory pressure (PIP), mean airway pressure (MAP), positive-end expiratory pressure (PEEP) and gas analysis (yellow) - inspiratory oxygen concentration (FiO_2 jet), the ventilated patient's oxygen concentration (FIO_2AW), intermittent end tidal CO_2 ($etCO_2$), were laterally attached to the convertor (Figure 4).

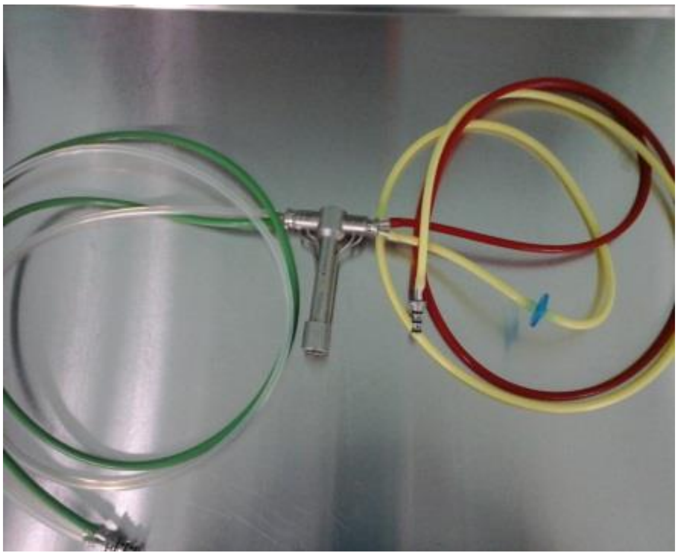

Fig. 4. The four catheters attached to the convertor

After choosing the BRO mode, the ventilator automatically displays set parameters based on a body weight algorithm. These parameters are: for HF ventilator emission pressure - $P_{HF[bar]}$=0.1-2 bar, ventilation frequency – f [1/min]=50-1500/min, inspiratory/expiratory ratio I:E=1:5-3:1 and for NF ventilator emission pressure - $P_{NF[bar]}$=0.1-3.5 bar, ventilation frequency – f [1/min]=1-100/min, inspiratory/expiratory ratio I:E=1:5-3:1 (Figure 5).

Fig. 5. Automatically selected parameters in bronchoscopy mode

Subsequently, these parameters can be adjusted in order to achieve an optimal oxygenation and ventilation.

The TwinStream jet ventilator allows intermitent $etCO_2$ measurement. By selecting $etCO_2$ icon on the main screen, HF stops automatically, NF runs for five cycles and, after $etCO_2$ assessment, both types of JV start again.

We set a safety upper limit for the peak airway pressure of 25 mmHg.

When the procedure was completed the neuromuscular block was reversed with sugammadex (dose dependent on TOF values), propofol TCI was stopped and the jet ventilator was switched off. The patients were ventilated by face mask or LMA using the circle circuit till adequate spontaneous breathing.

Intra-anaesthetic monitoring

The following intra-anaesthetic monitoring (Infinity C700 Draeger) was used in all patients:

- hemodynamic monitoring - ECG 2 leads (DII, V4), heart rate (HR), continuous ST segment monitoring, noninvasive blood pressure (BP)
- oxygenation monitoring - peripheral oxygen saturation (SpO_2)
- hypnosis monitoring - bispectral index (BIS)
- neuromuscular function monitoring – train of four (TOF).

Ventilator monitoring (Twin Stream, Carl Reiner GmbH) consisted of peak inspiratory pressure (PIP), mean airway pressure (MAP), positive-end expiratory pressure (PEEP), inspiratory oxygen concentration (FiO_2 jet), the ventilated patient's oxygen concentration (FIO_2 AW), intermittent end tidal CO_2 ($etCO_2$).

After complete recovery all patients were transferred to Post Anaesthesia Care Unit.

All recorded parameters are presented as mean values +/-standard deviation.

Results and discussion

In the present study we report our first case series of cancer patients scheduled for diagnostic and interventional bronchoscopy managed with TIVA-TCI and SHFJV. The procedures consisted in flexible and rigid bronchoscopy, the majority of our patients (n=19/24) undergoing EBUS-TBNA. In one lung cancer suspected patient proposed for this procedure we identified a bronchial foreign body extracted with rigid bronchoscopy in another session.

EBUS-TBNA is currently used for pre-operative lymph node staging of lung cancer, post-operative evaluation, diagnosis of centrally located intrapulmonary tumors or mediastinal and hilar adenopathy [9]. Being less invasive, safer than and as accurate as surgical staging in lung cancer patients, EBUS-TBNA is considered the test of first choice to confirm mediastinal lymph node involvement [10]. This procedure is generally performed under general anaesthesia to allow for a more precise ultrasound probe movement and needle position [11].

Our anaesthetic protocol consisted of propofol TIVA-TCI Schnider model aiming during induction for Ce=4.0-6.0 µg/ml according to patients ASA status. During the maintenance, an adequate level of hypnosis (BIS between 40 and 60) was obtained with a mean propofol Ce=3.1 (+/-0.6) µg/ml. In these circumstances hemodynamic parameters - heart rates and mean arterial pressures had no major variation being +/-10-20% from preoperative values.

The choice of anaesthetic technique and anaesthesia depth are continuous challenges for anaesthetists. Total Intravenous Anaesthesia is the preferred technique in an open circuit circumstances avoiding environment pollution. During inhalational anaesthesia, end tidal anaesthetic concentration correlates with effect site (brain) concentration and guides variation of hypnosis depths. By contrast, TIVA with propofol at a constant infusion rate results in an unpredictable and often suboptimal site effect concentration. We used in our patients propofol target controlled infusion. The major advantage of this technique is the continuous automatic adjustment of infusion rate in order to maintain the estimated plasma/effect site concentration equal to the set level. Despite the improved efficacy and safety profile of TIVA-TCI, propofol cerebral concentration is just estimated (not measured) according to a presumed pharmacokinetic models. In this respect, we used hypnosis monitoring with BIS as a component of our anaesthetic protocol. This approach is supported by the last UK National Audit Project (NAP5) on Accidental Awareness during General Anaesthesia in the United Kingdom and Ireland recommending BIS monitoring in all TIVA with muscle relaxants patients [12].

We varied propofol Ce (more than 2 µg/ml) in order to maintain BIS in a range of 40-60, aiming to avoid intra-anaesthetic awareness and to optimize anaesthetic depth according to procedural phases.

Currently available TIVA-TCI pumps use 2 pharmacokinetic models - Marsh and Schnider. The Marsh model assumes that the central compartment volume is directly proportional to weight only. The age is entered, but not used in the calculations, resulting in lack of accuracy. In Schnider model, lean body mass (estimated according to height and weight) and age are used to calculate doses and infusion rates resulting in better accuracy. For this reason, Schnider model results in lower propofol doses and should be preferred in elderly patients [13].

In our case series, the diagnosis or staging procedures were scheduled in lung cancer patients with reduced respiratory reserves. Our anaesthetic technique using propofol TCI Ce ensures fast recovery without residual sedation.

Muscle relaxants were used in all our patients. For flexible bronchoscopy with EBUS-TBNA the use of LMA affords easy bronchial tree access, optimal operator comfort and avoids endotracheal intubation. At the end of procedure rocuronium was reversed with sugammadex, a very efficient antagonist fulfilling the requirements for fast recovery.

Another advantage of TIVA with propofol is the lower interference with the immune system. Along with the ongoing debate regarding the effect of anaesthetic and analgetic drugs on malignancy recurrence, reported data tend to support the use of propofol based anaesthesia due to a lesser immune suppressive effect [14-16].

In the present case series we used for the first time the recently introduced jet ventilation – SHFJV. During conventional ventilation, tidal volumes exceed anatomical and equipment dead space and gas exchange is largely related to bulk flow of gas to the alveoli. In high frequency ventilation the tidal volumes are smaller than total dead space. Therefore, bulk flow only partially contribute to gas exchange along with alternative mechanisms: pendelluft - redistribution of inspired gas from full, fast-filling units to slower-filling lung units, convective streaming or Taylor dispersion – diffusion of the molecules with high axial velocities from central to lateral zones and cardiogenic mixing – air agitation in surrounding lung tissue by the heart beats [17-20]. The limits of high frequency ventilation are related to the open ventilation system – lack of CO_2 removal, airway pressure monitoring, tidal volume control and gas dryness.

By superposition of the normal frequency on high frequency ventilation, SHFJV increases minute ventilation and allows CO_2 removal [21]. It may also increase positive end expiratory pressure and end-expiratory volume improving oxygenation [22], with low risk of barotrauma and air trapping. In an animal model, end-expiratory and tidal volumes determined by opto-electronic plethysmography were greater and gas exchange was improved with this technique [23]. Another advantage is lung protection as a result of low tidal volume ventilation and relative chest immobility.

In our patients, in order to improve oxygenation, we increased the inspiratory oxygen fraction, NF and HF ventilation emission pressure, the frequency of HF and the I:E ratio. The $PaCO_2$ was maintained by increasing emission pressure and frequency of NF ventilation or by decreasing the frequency and I:E ratio of HF ventilation. Using a variable FiO_2=0.5 - 1 and frequency on HF=400-550/min, SpO_2 was maintained stable with a mean intra-anaesthetic value of 98.5%. $EtCO_2$, intermittently measured every 5 minutes, had a mean value of 32 (+/-5.4) mmHg, using a respiratory rate on NF=10-14/min. Our results confirm other published data showing normocapnia in SHFJV patients [24].

Recorded airway pressures during the jet ventilation - PIP, MAP, PEEP - varied according to the patient pre-existent lung pathology and procedural particularities. We set a safety upper limit for the peak airway pressure of 25 mmHg in order to avoid barotrauma. The Twin Stream ventilator, an electronic controlled multimode high frequency ventilator with two jet plateau, is simple to operate, has a quick setup and an intuitive user interface. Automatic initial settings calculated by body weight, extended monitoring capabilities including airway pressure monitoring and automatic manoeuvre for $etCO_2$ measurement, reduced risk of barotrauma with alarm pressure and stop ventilation, are greatest advantages. We recorded no intra-anaesthetic or post-interventional complications.

Conclusion

In order to circumvent challenges associated with diagnostic or interventional bronchoscopy in cancer patients we developed and applied an anaesthetic protocol in combination with Superimposed High Frequency Jet Ventilation. Our protocol enables a fast induction – fast recovery anaesthesia, cardiovascular stability and lowest immune suppression. SHFJV is a safe and effective method of ventilation in open system, maintaining good oxygenation and adequate CO_2 removal and is highly suitable for endoscopic interventions. The results of our case series analysis point towards the efficacy and safety of these techniques, operator comfort and facilitation of the procedure.

Disclosure

The authors have no conflict of interests to declare.

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