Tecniche di sedazione procedurale per Fibrobroncoscopia

Massimiliano Sorbello, MD

Anesthesia and Intensive Care
AOU Policlinico Vittorio Emanuele
University Hospital
Catania, Italy

Coordinatore GdS SIAARTI Gestione Vie Aeree
EAMS Board– Science Officer
ESA SC11 Respiration and Airway Management
“Awake FOB: which sedation?”

“Balance between patient comfort, good intubating condition and maintaining ventilation and patient’s airways”
• There is an equal safety record of sedation vs no sedation in bronchoscopy.

• Patients’ satisfaction and procedure tolerance are significantly improved with sedation.

• Sedation is suggested in all patients undergoing bronchoscopy unless contraindications exist.
Which patients?

- Pediatric
- Non-cooperative
- Reluctant or refusal for awake technique
- Rescue intubation after awakening
- *Dedicated airway technique*
This is sedation regimen:
Sedation for flexible bronchoscopy: current and emerging evidence

“**There is no standardised practice for the use of sedation in bronchoscopy with a good deal of variation among physicians regarding the use of pre-procedure medication and pharmacological sedatives**”.

José RJ. ERR 2013.

**TABLE 2** Pre-sedation flexible bronchoscopy checklist

<table>
<thead>
<tr>
<th>Item</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient identifier (name, date of birth)</td>
<td></td>
</tr>
<tr>
<td>Consent form signed</td>
<td></td>
</tr>
<tr>
<td>Responsible adult available to escort the patient post-procedure</td>
<td></td>
</tr>
<tr>
<td>Adequate fasting period</td>
<td></td>
</tr>
<tr>
<td>Allergies</td>
<td></td>
</tr>
<tr>
<td>Hepatic and renal function (if the clinical history suggests these could be abnormal)</td>
<td></td>
</tr>
<tr>
<td>Observations (vital signs)</td>
<td></td>
</tr>
<tr>
<td>Continuous pulse oximetry available</td>
<td></td>
</tr>
<tr>
<td>Intravenous access functioning</td>
<td></td>
</tr>
<tr>
<td>Medications checked</td>
<td></td>
</tr>
<tr>
<td>Resuscitation trolley available with emergency drugs</td>
<td></td>
</tr>
<tr>
<td>Reversal drugs available (flumazenil and naloxone)</td>
<td></td>
</tr>
<tr>
<td>Oxygen available (including variety of oxygen delivery devices)</td>
<td></td>
</tr>
<tr>
<td>All staff ready for the procedure to commence</td>
<td></td>
</tr>
</tbody>
</table>

Data from [22].
Moderate sedation

- The depth of sedation should always be monitored throughout the procedure and documented using the Ramsay scale.
- For moderate sedation a depth of sedation should not be greater than that of level 3.

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Ramsay sedation scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Patient is anxious and agitated or restless, or both</td>
</tr>
<tr>
<td>2</td>
<td>Patient is cooperative, oriented and tranquil</td>
</tr>
<tr>
<td>3</td>
<td>Patient responds to commands only</td>
</tr>
<tr>
<td>4</td>
<td>Patient exhibits brisk response to light glabellar tap or loud auditory stimulus</td>
</tr>
<tr>
<td>5</td>
<td>Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus</td>
</tr>
<tr>
<td>6</td>
<td>Patient exhibits no response</td>
</tr>
</tbody>
</table>
Extent of sedation
(minimal, moderate, deep, or general anesthesia)

- Procedural settings (office, ICU, or operating room).
- Complexity and duration of the procedure (advanced diagnostic or therapeutic bronchoscopy).

- Patient? VENTILABILITY!!!
Benzodiazepines
Effects

- Antianxiety
- Anterograde amnesia
- Sedation

- Less discomfort vs opioid
- Less respiratory depression vs opioid
- Longer time of recovery vs opioid

- Midazolam 0.06/0.07 mg*kg\(^{-1}\)
- Higher doses = no advantage

- Antagonist available
The use of combination of benzodiazepines and opioids is suggested because of synergistic effects on patient tolerance during the procedure and the added antitussive properties of opioids.

The suggested preferred opioid agent in bronchoscopy is fentanyl because of its quick onset of action, rapid peak effect, and relatively short duration of effect (antagonist available).
Context-Sensitive half time

![Graph showing context-sensitive half times for different opioids](image)

- Fentanyl
- Alfentanil
- Sufentanil
- Remifentanil
Metabolism

Midazolam, Fentanyl, Alfentanyl, Ketamine

CYP450 (CYP34A)

- Age
- Hepatic failure
- Drug abuse
- Drugs (anti-retroviral, Ketoconazole, Fluconazole, Erythromicin, Diltiazem, Cimetidine ..)
TCI for Fiberoptic intubation

- 60 patients, no premed.
- TCI titrated to no or little response

Lallo, Anesth Analg 2009
Propofol

<table>
<thead>
<tr>
<th>Year</th>
<th>Reference</th>
<th>Type</th>
<th>n</th>
<th>Details</th>
<th>Conclusions</th>
<th>Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td>Lee et al.</td>
<td>Prospective RCT</td>
<td>30</td>
<td>Propofol 1 mg/C1 kg - 1 bolus then 1 mg/C1 kg - 1/C1 hr - 1</td>
<td>Patients in the propofol group were more sedated despite no differences in coughing, intubating conditions, or time taken for the procedure.</td>
<td>None</td>
</tr>
<tr>
<td>2008</td>
<td>Rai et al.</td>
<td>Prospective RCT</td>
<td>24</td>
<td>TCI Propofol Ce 1.3 (1-1.6) μg·mL⁻¹ vs TCI Remifentanil Ce 3.2 (2.8-3.5) ng·mL⁻¹ *Midazolam 1-2 mg in both groups</td>
<td>Remifentanil provided better intubating conditions (faster intubation and less coughing) Better patient tolerance but associated with a high incidence of recall (60%).</td>
<td>Severe coughing in one patient necessitated a second attempt in the propofol group</td>
</tr>
<tr>
<td>2009</td>
<td>Lallo et al.</td>
<td>Prospective RCT</td>
<td>60</td>
<td>TCI Propofol Ce 3.9 (1.4) μg·mL⁻¹ vs TCI Remifentanil Ce 2.4 (0.8) ng·mL⁻¹</td>
<td>Intubating conditions good in both groups Remifentanil provided better patient cooperation Patients in the propofol group had more coughing, were significantly more sedated and less cooperative Recall more frequent with remifentanil (96%) compared with propofol (50%).</td>
<td>1 patient in propofol group agitated and developed airway obstruction and hypoxia</td>
</tr>
<tr>
<td>2012</td>
<td>Zhang et al.</td>
<td>Prospective RCT</td>
<td>36</td>
<td>TCI Propofol Ce 5.83 (1.46) μg·mL⁻¹ vs TCI Remifentanil Ce 3.74 (0.31) ng·mL⁻¹ *Limited topical anesthesia in both</td>
<td>Remifentanil provides safe intubating conditions Propofol was unsuitable</td>
<td>&gt;88% of patients in the propofol group became unresponsive, and 20% desaturated</td>
</tr>
<tr>
<td>2010</td>
<td>Tsai et al.</td>
<td>Prospective RCT</td>
<td>40</td>
<td>Dexmedetomidine 1.0 μg/C1 kg - 1 over 10 min vs TCI Propofol Ce 3.6 μg·mL⁻¹</td>
<td>Both provided satisfactory conditions. DEX group had fewer airway events and more hemodynamic stability but higher recall.</td>
<td>1 patient in the propofol group agitated and developed airway obstruction and hypoxia</td>
</tr>
<tr>
<td>1990</td>
<td>Randell et al.</td>
<td>Prospective RCT</td>
<td>30</td>
<td>Diazepam 0.1 mg/C1 kg - 1 and alfentanil 20 μg/C1 kg - 1 vs Diazepam 0.1 mg/C1 kg - 1</td>
<td>Heart rate and BP increases were attenuated with alfentanil. Systolic and diastolic BP increased 24% and 48%, respectively, without opioid.</td>
<td>1 patient in the DEX group exhibited gross limb movement</td>
</tr>
</tbody>
</table>
Remifentanil

<table>
<thead>
<tr>
<th>Year and reference</th>
<th>Type</th>
<th>n</th>
<th>Details</th>
<th>Conclusions</th>
<th>Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belda et al. 2011</td>
<td>Prospective RCT</td>
<td>75</td>
<td>TCI Remifentanil Ce 2.4 (0.4) ng·mL⁻¹</td>
<td>Remifentanil TCI provides optimal conditions for AFOI. Addition of ketamine to TCI remifentanil did not offer any advantages. Ketamine alone is not adequate sedation for AFOI</td>
<td>High incidence of cough (60%), agitation, and inadequate sedation in the ketamine only group. I patient in the TCI remifentanil + ketamine group oversedated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>vs TCI Remifentanil Ce 2.1 (0.8) ng·mL⁻¹ + Ketamine 0.3 mg·kg⁻¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>vs Ketamine 0.3 mg·kg⁻¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yeganeh et al. 2010</td>
<td>Prospective RCT</td>
<td>22</td>
<td>TCI Remifentanil Ce 0.8 ng·mL⁻¹</td>
<td>Preparation time shorter in the TCI group. Vital signs more stable in TCI group. More recall and pain in the manual group TCI provides better conditions and is easier to use</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>vs Remifentanil infusion loading dose 0.75 µg·kg⁻¹ followed by infusion of 0.075 µg·kg⁻¹·min⁻¹</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

All drugs given via the intravenous route unless stated otherwise. RCT = randomized controlled trial; TCI = target-controlled infusion; Ce = effect-site (range or SD) concentration; AFOI = awake fibreoptic intubation; DEX = dexmedetomidine; BP = blood pressure.
Role of novel drugs in sedation outside the operating room: dexmedetomidine, ketamine and remifentanil

CONCLUSIONS

- Sedation outside the operating room necessitates the use of well tolerated drugs, devoid of respiratory depression, airway obstruction or cardiovascular compromise.

- Dexmedetomidine seems devoid of respiratory adverse effects, bradycardia and hypotension might limit its use together with a slow onset and recovery time.

- Ketamine is very efficacious for sedation, but still generates psychogenic side-effects during emergence. As part of a multimodal pain treatment protocol, however, it might impact patient’s long-term outcome.

- Remifentanil as a powerful and short-acting opioid is a good option for sedation in painful diagnostic or therapeutic procedures.

One study (498 FOB) using PPF outside OR 6.6 % complications
Alpha-Adrenoceptor Agonists

- Norepinephrine
- Epinephrine
- Dopamine
- Tizanidine
- Clonidine
- MPV-2426
- Mivazerol
- Guanfacine
- Guanabenz
- Medetomidine
- Dexmedetomidine
Dexmedetomidine

The role of dexmedetomidine for sedative drugs has been coined to describe the depression associated with traditional anaesthesia techniques. The term 'immunosedation' has been used to describe the effects of between 25% and 70% of drugs. The resultant reduction in doses of volatile anaesthetic and opioid may be seen in its beneficial effect for a plethora of postoperative problems. There are significant decreases in the incidence of delirium and agitation. The resultant reduction in doses of volatile anaesthetic and opioid may be seen in its beneficial effect for a plethora of postoperative problems.

Pharmacokinetic limitations

Dexmedetomidine has a slow onset time and a peak effect is at least 10 minutes after the attainment of adequate plasma levels of the drug. As a generally smooth hypnotic, it is immediately apparent that dexmedetomidine is an adjunct to more conventional general anaesthesia techniques. Dexmedetomidine has MAC-sparing activity when the drug is used as an anaesthetic adjunct to more conventional general anaesthesia techniques. Dexmedetomidine has MAC-sparing activity when the drug is used as an anaesthetic adjunct to more conventional general anaesthesia techniques. Dexmedetomidine has a long duration of effect. Analogous to fentanyl, the offset of action is also strongly concentration dependent. In both healthy subjects and critically ill patients, the text is sensitive. In both healthy subjects and critically ill patients, the text is sensitive.

When and how would I use it?

Dexmedetomidine is a highly useful drug. The compound atipamezole, a 2-adrenoceptor antagonist would be very helpful. I would be less likely to use it for sedation if: (i) rapid changes in depth of sedation were required; (ii) the patient was dependent on sympathetic control of nociception; (iii) reliable amnesia is required; or (iv) a strong noxious stimulus is anticipated. I would consider it for procedural sedation if I was concerned about risks of respiratory embarrassment (e.g. obesity, the elderly, those patients on ventilators, and the operating theatre).

For sedation in the intensive care unit results in improved mortality in septic patients. It is very easy to overshoot the brain and spinal cord.

Sedated

Wakeful

0 20 40 60 80 100 120 140 160 180

Time (min)

0 0.5 1 1.5 2 2.5

C_e (ng.ml^{-1})

0.5 µg.kg^{-1}

1.0 µg.kg^{-1}

2.0 µg.kg^{-1}

Fig. 1. Assuming that significant prolonged sedation and bradycardia, might be expected to last for some hours. This is therefore a short summary of my practice, distilled into a decade. This is therefore a short summary of my practice, distilled into a decade. This is therefore a short summary of my practice, distilled into a decade. This is therefore a short summary of my practice, distilled into a decade. This is therefore a short summary of my practice, distilled into a decade.
Dexmedetomidina

Effect of different loading doses on sedation

- Higher loading doses may lead to more rapid sedation
- No clinically significant differences between groups

**Table 3. Complications, Drug Use, Minimal BIS and Time to Reach BIS 80**

<table>
<thead>
<tr>
<th>Complication</th>
<th>Group H</th>
<th>Group L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bradycardia</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Hypoxemia</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Hypotension</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>BISmin</td>
<td>54.1 ± 17.8</td>
<td>57.7 ± 15.5</td>
</tr>
<tr>
<td>Time to reach BIS 80 (sec)</td>
<td>145.7 ± 213</td>
<td>56.7 ± 71</td>
</tr>
</tbody>
</table>

Values are mean ± SD or number of patients. There are no significant differences between two groups. Group L: loading dose 0.5 µg/kg, Group H: loading dose 1.0 µg/kg. BISmin: Lowest value of BIS during the study.

**Fig. 1.** Bispectral index during sedation. *P < 0.05 compared to $T_0$, $P < 0.05$ between two groups, Group L: loading dose 0.5 µg/kg, Group H: loading dose 1.0 µg/kg. $T_0$: start of anesthesia, $T_L$: after loading, $T_{10}$: 10 minutes after $T_L$, $T_{20}$: 20 minutes after $T_L$, $T_{30}$: 30 minutes after $T_L$. 
Procedural FOB dosing

- All patients will receive an intravenous loading dose of dexmedetomidine
  1 mcg * kg⁻¹ over 10 min followed by a continuous infusion of
  0.2-0.7 mcg *kg⁻¹* h⁻¹

Clinical Study

Dexmedetomidine versus Remifentanil for Sedation during Awake Fiberoptic Intubation

Davide Cattano, Nicholas C. Lam, Lara Ferrario, Carmen Seitan, Kash Vahdat, Darrell W. Wilcox, and Carin A. Hagberg

This study compared remifentanil and dexmedetomidine as awake fiberoptic intubation (AFOI) anesthetics. Thirty-four adult ASA I-III patients were enrolled in a double-blinded randomized pilot study to receive remifentanil (REM) or dexmedetomidine (DEX) for sedation during AFOI (nasal and oral). Thirty patients completed the study and received 2 mg midazolam IV and topical anesthesia. The REM group received a loading dose of 0.75 mcg/kg followed by an infusion of 0.075 mcg/kg/min. The DEX group received a loading dose of 0.4 mcg/kg followed by an infusion of 0.7 mcg/kg/hr. Time to sedation, number of intubation attempts, Ramsay sedation scale (RSS) score, bispectral index (BIS), and memory recall were recorded. All thirty patients were successfully intubated by AFOI (22 oral intubations/8 nasal). First attempt success rate with AFOI was higher in the REM group than the DEX group, 72% and 38% (P = 0.02), respectively. The DEX group took longer to attain RSS of ≥3 and to achieve BIS <80, as compared to the REM group. Postloading dose verbal recall was poorer in the DEX group. Dexmedetomidine seems a useful adjunct for patients undergoing AFOI but is dependent on dosage and time. Further studies in the use of dexmedetomidine for AFOI are warranted.
Dexmedetomidine

First choice for sedation:

• Risk for respiratory embarassment (obesity, airway obstruction)
• Restlessness (elderly, pt on/or withdrawing from psychoactive drugs)

Second choice or combination:

• Rapid changes in dept of sedation
• Reliable amnesia (?)
• Strong noxious stimulus
• Emergency Dept?
Sleep Apnea Patients

- Morbid obesity, at risk for aspiration
- Difficult IV access
- Systemic + pulm HTN, cor pulmonale
- Postop airway obstruction + ventilatory arrest with anesthetic drugs
  - ↓ upper airway muscle activity
  - inhibition of normal arousal patterns
  - upper airway swelling from laryngoscopy, surgery, intubation

Dexmedetomodine

- Anesthetic adjunct to minimize opioid + sedative use
Perioperative Dex Infusion Protocol

Example: 70 kg patient. Assess BP, HR, volume status

Hypovolemic

2 mL Dex in 48 mL 0.9% saline = 200 ug/50 mL, or 4 ug/ml
Start at 40 mL/hr
Stop load if ↓ HR

Usual load: 25 to 35 ug or 6 to 9 mL over 10-15 min

Normovolemic

Volume preload 500 to 1000 cc LR

Local Anesthesia: SAYGO

Monitor BP/HR throughout
If bradycardia, ↓ infusion

Maintenance: 0.2 to 0.7 ug/kg/hr [4 to 12 mL/hr]

500 to 1000 cc LR

500 to 1000 cc LR
**Dexmedetomidine for the management of awake fibreoptic intubation (Review)**

He XY, Cao JP, He Q, Shi XY

---

**Main results**

We identified four randomized controlled trials (RCTs), which included 211 participants. The four trials compared dexmedetomidine with midazolam, fentanyl, propofol or a sodium chloride placebo, respectively. The trials showed low or unclear risk of bias primarily because information provided on allocation concealment and other potential sources of bias was inadequate. Owing to clinical heterogeneity and potential methodological heterogeneity, it was impossible to conduct a full meta-analysis. We described findings from individual studies or presented them in tabular form. Limited evidence was available for assessment of the outcomes of interest for this review. Results of the limited included trials showed that dexmedetomidine significantly reduced participants’ discomfort with no significant differences in airway obstruction, low oxygen levels or treatment-emergent cardiovascular adverse events noted during AFOI compared with control groups. When the search was rerun (from May 2012 to November 2013), it was noted that four studies are awaiting assessment. We will deal with these studies when we update the review.

**Authors’ conclusions**

Small, limited trials provide weak evidence to support dexmedetomidine as an option for patients with an anticipated difficult airway who undergo AFOI. The findings of this review should be further corroborated by additional controlled investigations.
Conscious sedation for awake fibreoptic intubation: a review of the literature

La sédation consciente pour l’intubation fibroscopique vigile : revue de la littérature

Kevin D. Johnston, MBChB (Hons) · Mridula R. Rai, MD

both anxiolytic and analgesic properties. The ideal choice of drug may vary depending on the patient and the indication for AFOI.

Conclusion There is good evidence to support the use of two drugs in particular, remifentanil and dexmedetomidine. Each has certain unique characteristics that make them an attractive choice for an AFOI.