Remifentanil as Sole Agent for Awake Fibre Optic Intubation

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Awake fibre optic intubation (AFOI) has been performed successfully for many years facilitated by various sedation and local anaesthetic techniques. So why bother with remifentanil?

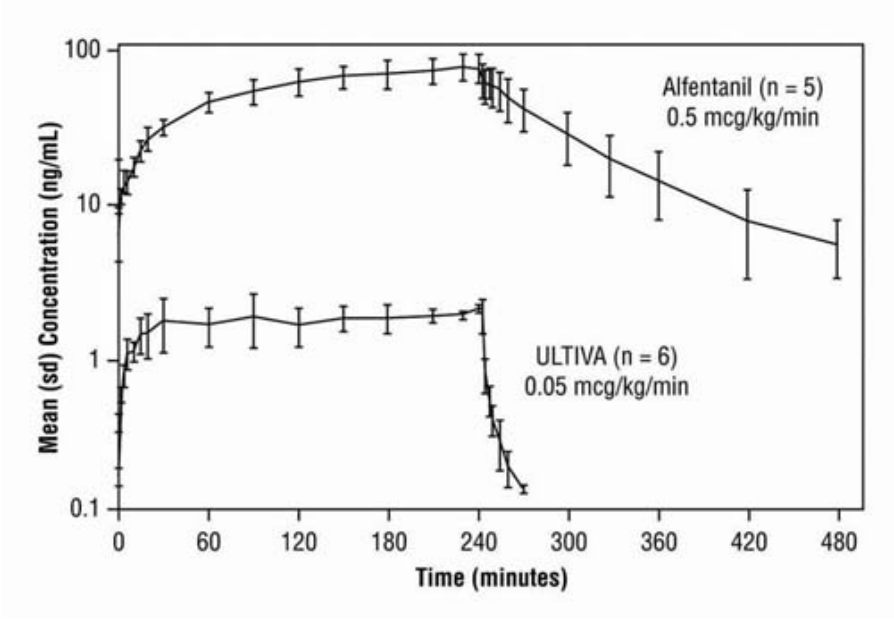
Put simply, we believe remifentanil is the best method of sedation, for both anaesthetist and patient. The aim of this article and workshop is to convince you of its efficacy and safety encouraging you to be confident of learning to use it yourself.

Pharmacology of remifentanil

Remifentanil hydrochloride is a novel evanescent opioid presented as a sterile, preservative free, white lyophilized powder in 1, 2 and 5mg vials. It requires reconstitution with water or saline and is stable for 24 hours. It is in the same structural family as fentanyl and the other phenylpiperidines.

It is a selective μ opioid receptor agonist, of higher potency than alfentanil, but with pharmacological effects that essentially parallel those of alfentanil and other opioids in this class. Remifentanil's onset of action is similar to that of alfentanil, but has a much more rapid offset because unlike other opioids, which are metabolized hepatically and excreted renally, remifentanil is rapidly hydrolyzed by nonspecific plasma and tissue esterases.

Remifentanil's context-sensitive half-life is very short (3 to 4 minutes) and independent of the duration of its infusion. These characteristics facilitate titration of dose to effect and also allow the use of very high doses (ED99) without fear of prolonging recovery. There is no residual opioid activity 5 – 10 minutes post discontinuation of the infusion (Its effects can also be reversed with naloxone).



Remifentanil can be seen to possess many of the characteristics of the 'ideal sedative'. Its unique pharmacology confers the valuable attributes of extreme brevity of action, precise and easily titratable (non cumulative) effects plus rapid recovery after cessation of its infusion. In practice this means cooperative, less sedated patients[1].

It should be stressed that remifentanil has no amnesic properties and patients do possess recall of their intervention. Clinicians should carefully weigh up the pros and cons of administering a small dose of benzodiazepine, as this will amplify remifentanil's respiratory side effects. In our experience recall is not a problem. Patients do not view recalled events as distressing[1,2]. Vennila et al[1] showed that although 15/20 patients undergoing nasal AFOI recalled the procedure, discomfort was reported as absent (n=10) or mild (n=6) with a only minority reporting it as moderate (3) or severe (n=1). Patients coming for repeat procedures in our institution are not 'put off' by the experience, and in many cases request this method, as in their experience it is far superior to what they had before (midazolam and topicalised lidocaine)[3].

Side effects of remifentanil when used for sedation

Side Effect	Treatment
Bradycardia, Hypotension	Fluid preload Slow bolus Atropine
Apnoea, hypoxia	Nasal O_2 Slow bolus Stop infusion Remind patient to breathe IPPV Naloxone
Slow onset	Running drip Non-siphoning valve Care with elderly
Chest wall rigidity	Slow bolus Stop infusion Benzodizapine Naloxone Muscle relaxant

Remifentanil's side effects are predictable and so should be easily anticipated, ideally prevented or rapidly recognized and treated. They are secondary to the size and speed of administration of the initial bolus dose plus subsequent infusion rate and are more likely in the elderly or debilitated. All can be avoided by a small slow bolus dose and low initial infusion rate (increasing in small increments), especially in 'at risk' patients.

"Spray As You Go" (SAYGO) topical anaesthesia?

Remifentanil is such a potent analgesic that the indications for use of topical anaesthesia as a SAYGO technique are extremely small.

In the Mersey region, we have been performing AFOI successfully with remifentanil as sole sedating agent for several years[1]. We abandoned the use of topical local anaesthesia (LA) to the airway as we found it messy, unpredictable and unpleasant for both the patient and anaesthetist: SAYGO takes more than three times as long as when using remifentanil[1, 4].

Several papers have shown that SAYGO reduces the dose of remifentanil needed for AFOI[4-5]. However, remifentanil has such easily treated side effects we believe this to be no argument for its inclusion as SAYGO is associated with acute airway obstruction [6-8]. The mechanism is probably due to the loss of upper airway muscle tone, exacerbated by deep inspiratory effects whist the patient panics because of sudden dyspneoa. Local anaesthesia may cause this directly by precipitating laryngospasm, or indirectly by ablating the afferent loop of local airway reflexes that maintain dynamic upper airway patency.

The usual maximum dose for SAYGO lidocaine has been quoted as 4mg/kg but a dose of 9mg/kg has been reported[4,9]. However, topicalisation is frequently associated with toxicity as the safe dose is easily exceeded in practice. The symptoms and signs of LA toxicity in terms of neurological symptoms have been reported in 37% (out of 200) participants in a course in Norwich where anaesthetists learn AFOI under LA[9]

SAYGO also readily precipitates coughing, which, although usually just a nuisance, can exacerbate an already precarious airway problem[10]. Lastly, the fact that a patient's airway is anaesthetized post operatively means fasting has to be continued.

Remifentanil sedation for AFOI

Having outlined the problems with SAYGO as a technique, let's consider the alternative: "conscious sedation": a "minimally depressed level of consciousness that retains the patient's ability to maintain a patent airway independently, continuously plus the ability to respond to physical or verbal stimulation"[11]. We believe remifentanil is the best agent to provide this state of conscious sedation because of its unique pharmacology.

Reusche [12] was the first to publish a report of the use of remifentanil to facilitate AFOI. He described a straightforward intubation with no coughing, gagging or bucking in a patient presenting with Ludwig's angina; all points recognized today as hallmarks of this agents use in AFOI. Since then, many papers have reported remifentanil's efficacy as an integral part of numerous different sedation techniques for AFOI.

Puchner[5] compared standard midazolam (1-10mg) and fentanyl (1.5μg/kg) sedation with remifentanil (0.1μg/kg bolus plus an infusion commencing at 0.25μg/kg/min increasing in 0.05μg/kg/min increments giving final rates between 0.25-0.5μg/kg/min). 37 patients were allocated to each group and all patients received a spray of 4% lidocaine and nasal vasoconstrictor (xylometazolin). The authors reported that remifentanil "seems to improve intubation conditions and the quality of the procedure" in that remifentanil produced 'conscious sedation' with better reflex suppression and ease of control of the level of sedation compared with midazolam and fentanyl. Higher recall with remifentanil as a sole agent was noted.

Machata[13] compared high dose remifentanil sedation (1.5μg/kg bolus plus 0.15 μg/kg/min infusion) with low dose remifentanil sedation (0.75μg/kg bolus plus 0.075μg/kg/min infusion) in 24 patients having a nasal AFOI. The technique included supraglottic and glottic lidocaine spray. Both study arms blunted airway reflexes effectively and ensured adequate intubating conditions, patient comfort and sedation. However, the high dose regimen provided more sedation, less coughing and less recall.

Rai[2] published a double blind randomized controlled trial comparing sedation with target controlled infusions (TCI) of remifentanil with propofol respectively for AFOI. Patients in both arms of the study

received nasal cocaine, atomized oro-pharyngeal lidocaine plus glottic lidocaine spray. Remifentanil was used at a dilution of 50μg/ml for the Minto protocol with an initial effect site concentration of 3ng/ml increasing in 0.5ng/ml increments to give effect site concentrations at intubation of 3.2 (2.8-3.5) ng/ml. Propofol 1% was used in the Schnider protocol with an initial effect site of 1μg/ml increasing in 0.5μg /ml increments to give effect site concentrations at intubation of 1.3 (1-1.6) μg /ml. Remifentanil was showed to produce significantly better conditions for AFOI due to its antitussive and analgesic properties. Recall was higher in the remifentanil group but did not appear to affect patient satisfaction.

Lallo[14] also compared TCI remifentanil with propofol for AFOI. Again, all patients received topical anaesthesia to nose pharynx and cords. Effect site concentrations at time of intubation were 2.4-±0.8 ng/ml for propofol and 3.9 ±1.4 μg/ml for remifentanil respectively. Patients receiving remifentanil had a wider vocal cord aperture at intubation and were found to be less sedated and more cooperative. Remifentanil seemed especially suitable to cases where patient cooperation and spontaneous ventilation are paramount. Lallo also commented on the superiority of TCI as a technique for giving remifentanil and highlighted the potential danger of over sedation with propofol as there is no reversal agent in such circumstances.

Cafiero[15]investigated the efficacy of combining remifentanil with propofol (in a ratio of 1:625) to reduce remifentanil requirements and provide amnesia coining the term “analgosedation”. The study looked at 20 patients with acromegaly having oral AFOI. Patients were premedicated with midazolam (0.03mg/kg), with initial effect site concentrations at 2.0 ±1.0 (1.5 to 3.5) μg/ml for propofol and 3.2 ± 0.3 (1-5) ng/ml for remifentanil. The infusions were subsequently increased incrementally during the procedure (remifentanil in 1ng steps and propofol by 1μg). An initial remifentanil effect site concentration of 3ng/ml was increased to 5ng/ml prior to railroading the tracheal tube. At the same time, the initial propofol effect site concentration of 2μg/ml increased to 3.5μ/ml. This achieved intubation within 4.4 ± 0.6 (4–6) minutes, with no adverse respiratory events and 85% of patients reporting no recall.

Xu et al[16] studied the median effective dose of remifentanil for oral AFOI along with midazolam and topicalised LA in 36 females undergoing plastic surgery. The bolus dose and infusion rate of remifentanil were

adjusted by a modified Dixon's up-and-down method. The ED (50) of remifentanil for successful AFOI was found to be bolus of 0.62 μ g/kg followed by continuous infusion at 0.062 μg/kg/min. This regimen provided patient safety and comfort, ensured adequate intubation conditions, maintained hemodynamic stability, and prevented negative recall of the procedure.

Vennila[1] described using TCI remifentanil as a single agent in 20 patients undergoing AFOI for dental abscess. The Minto protocol was employed with an initial effect site concentration of 1ng/ml rising in 0.5ng/ml increments to give an effect site concentration at time of endoscopy of 6.3 ± 3.87ng/ml. Once the fibrescope was positioned in the mid-trachea the effect site was increased (8.06 ± 3.52ng/ml) prior to railroading the tracheal tube. Despite these larger effect site concentrations no adverse desaturations or CVS events were reported with mild coughing was reported as the tracheal tube passed the vocal cords. Since this study we now employ an initial effect site concentration of 3ng/ml and increase in 1ng/ml steps (see appendix).

Remifentanil TCI sedation comparisons

	Venilla 2011	Rai 2008	Lallo 2009
Premedication	Nil	Midaz. 1-2mg Glyco. 0.2mg	Hydroxyzine 1-1.5mg.kg^{-1}
Topical LA	Nil	Yes	Yes
Initial Cet	1 ng/ml	3 ng/ml	1.5 ng/ml
Incremental Cet increase	0.5 ng/ml	0.5 ng/ml + SAYG	0.5 ng/ml + SAYG
Mean Cet	5 ng/ml	3.2 ng/ml	2.4 ng/ml
Maximum Cet	8 ng/ml	3.5 ng/ml	6 ng/ml *

Cet = effect site concentration

*Patient unintubatable due to anxiety.

In our opinion, although SAYGO +/- midazolam reduces the Cet needed to effect intubation they do not make the procedure any safer.

‘Mersey Method’ of remifentanil sedation for AFOI

From the outset, the most important thing is to consider whether the patient is suitable to undergo AFOI in terms of both their co-operation and comprehension of what is entailed. Although remifentanil provides excellent, easily reversible “conscious sedation” it has no anxiolytic and amnesic properties. The patient remains fully aware (and will have recall) of what is happening to them. In our opinion this is one of the methods advantages as the patient is ‘awake’ and not semi anaesthetized. Carefully consider the advisability or otherwise of co-administering a small dose of midazolam, as, should a patient decide that they do not like the experience, increasing the remifentanil will not prevent them from becoming uncooperative forcing the AFOI to be abandoned. In the worst case this could result in self extubation with the risk of epistaxis, which might have catastrophic implications in a critical airway.

Having deemed the patient suitable, spend time explaining why an AFOI is necessary and the whole process. Patients are frightened of the unknown; assuage this by describing who will be present, how they will be positioned, the order in which events will occur and the likely sensations that will be experienced. Emphasise how the patient’s actions can help (e.g. tongue protrusion) or hinder (e.g. talking) the proceedings.

Decide in advance where you will be doing the AFOI; theatre or anaesthetic room and what staff you need to help. A minimal requirement would be laryngoscopist, dedicated sedationist, ODP and a runner. Under certain circumstances you may wish to have a surgeon / scrub nurse primed and ready to perform a surgical airway should the AFOI fail. Always ensure that all your colleagues know what is going to happen, their role and what problems are likely to be encountered and how as a team these are to be dealt with. The ADAM website provides an excellent resource providing bespoke, detailed anaesthetic plans that dovetail well with the WHO checklist for this purpose.

To perform an AFOI we prefer the patient to be sat upright on the table. This means the laryngoscopist stands on a platform behind (or in front) of the patient. Set the remifentanil pump up (preferably as a TCI as it confers more controllability)[14] and connect it to the patient via a primed non-siphoning valve with a running drip. Ensure the cannula is well secured to prevent its accidental removal during the AFOI. Check the

scopes light source, focus and depth of field and antifog the lens prior to use. Warm the tube and only load it onto the fiberscope immediately prior to beginning the endoscopy.

Before commencing sedation prepare both nostrils with a topical vasoconstrictor (we use phenylephrine drops or spray). Ask the patient to blow their nose gently before instilling 3 drops/sprays into each nares. If not already done, perform a nasendoscopy to determine the best (most patent) nostril for intubation and then commence supplemental O_2 at 2 l/m via the other. The sedationist can now commence the remifentanil infusion (see appendix) maintaining verbal contact with the patient throughout. In our experience the patient may lose the respiratory drive despite being wide-awake. The sedationist should be alert to this possibility and monitor chest movements throughout and remind the patient to breathe as necessary. Gradually and incrementally increase the Cet until the patient appears drowsy but cooperative and then commence the AFOI. Once the trachea has been cannulated by the scope consider raising the Cet prior to advancing the tube. Remember to hand the scope to your ODA before using both hands to railroad the tube (this will make the process much easier and minimise the risk of accidently removing the scope before the tube is passed). Remember to orientate the TT tube's bevel relative to the turbinates, epiglottis and arytenoids to reduce the risk of epistaxis and hold up. Finally, check the tubes position relative to the carina before removing the scope (warn the patient in advance that they will not be able to breathe during these few *crucial* seconds). Connect the TT to a circuit and check for a CO_2 trace and bag movement before inducing anaesthesia. DO NOT inflate the tube's cuff until **after** the patient has been induced. Although a fantastic analgesic, remifentanil does not ameliorate the unpleasant sensation of the trachea being stretched as the cuff inflates. This can come as a sudden shock to patients who have had an otherwise comfortable experience and prompt a sudden loss of co-operation and possibly traumatic self extubation.

Appendix
Mersey remifentanil sedation protocol

	Remifentanil Infusion $\mu g.kg^{-1}.min^{-1}$	Remifentanil Infusion mls.hr 70kg	Remifentanil TCI Cet $ng.ml^{-1}$
Bolus µg/kg (1-2 mins)	0.5 -1 *	0.7 - 1.4*	
Initial infusion	0.1	8	1.5 – 3*
Incremental increase	0.05	4	1
Average Infusion	0.25	20	5
Maximal infusion	0.5-0.8	40-60	8

*Use the lower bolus dose in the elderly or patients with airway limitation. Patients having a 'difficult airway' with no airway limitation commence with the higher bolus dose of remifentanil.

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ADAM approach to the Anticipated Difficult Airway

This method helps you to tailor your assessment of the anticipated airway for the individual patient. It is an aide memoire for all the known clinical problems associated with difficult airway "scenarios" and works by matching these problems to the airway management options or "devices" available to you. The result is the "Responsive Contingency Plan" which you can analyse in detail to anticipate all the known problems anticipated for the case in hand. We teach this method on our local courses at Aintree and there is a website where all the information is available for use in the clinical setting. This has been up and running for over 2 years now and has currently been upgraded to version 2 to allow modifications in response to user feedback. The address for the website is –http://adam.liv.ac.uk (note "www" is not required)

ADAMWiki

This is a new website that is due for release in mid-November 2011. It will serve as an airway problem wiki and also as a manual for the ADAM method described above (for those who have not been on one of our ADAM courses). The idea of a wiki is to encourage contributions as well as to act as a knowledge resource. If you have any useful contributions and want to get your name on the "world wide web" this is your chance.

Airway Alert Card

This project has had DAS council support to be taken forward as a local initiative to issue alert cards to patients with airway problems. The details on how it will work will be found on the ADAMWiki site but this has the potential to go on to be a national system. Once a card has been issued, subsequent anaesthetists can use the ADAM reference number to look up previous airway managements and any comments made at the time.