Respiratory Medicine (1995) **89**, 53–56

Sedation for fibre optic bronchoscopy

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Most current sedative regimens for fibre optic bronchoscopy use an opioid, a benzodiazepine or a combination of both. This study compares midazolam (M) (a benzodiazepine), alfentanil (A) (an opioid) and a combination of both drugs (M+A).

One hundred and three patients were randomized in double-blind manner into groups M(35), A(33) and M+A(35). The number of coughs, number of additional aliquots of lignocaine and duration of the procedures were recorded along with oxygen desaturation. The patient's level of discomfort was assessed by patient and bronchoscopist and expressed as a visual analogue score.

There were significantly fewer coughs per minute in Group A compared with Group M ($P=0{\cdot}0053$), and significantly less lignocaine was required in Group A ($P=0{\cdot}005$) and in Groups M+A ($P<0{\cdot}002$) compared with Group M. There was no significant difference in the assessment of discomfort between the groups. There was a trend for Group M+A to desaturate more than the other two with a significant difference between desaturation in Group M+A and Group A ($P=0{\cdot}033$).

Alfentanil is a more effective anti-tussive agent than midazolam for outpatient fibre optic bronchoscopy. The combination of alfentanil and midazolam does not provide any better anti-tussive effect and may have the risk of a greater degree of desaturation secondary to increased sedation.

Introduction

Fibre optic bronchoscopy in the U.K. is usually performed with some form of sedation (1). Sixty per cent of patients in one study found bronchoscopy without sedation unpleasant or intolerable (2).

Ideally sedation should be safe, free from side-effects and have anxiolytic, amnesic and anti-tussive qualities. The choice of agents varies but usually a benzodiazepine, an opioid or a combination of both are used (3).

This study compares midazolam (M), a benzodiazepine with a very short half-life and alfentanil (A), an opioid which is rapidly metabolized to inactive products, and a combination of both drugs (M+A) as sedation for outpatient bronchoscopy.

Methods

Consecutive patients attending for outpatient bronchoscopy were randomized, after giving written and informed consent, to receive one of three varieties of sedation; none was given prior premedication.

Received 21 February 1994 and accepted in revised form 17 June 1994.

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Group M received intravenous midazolam titrated according to weight (2 mg if 50–60 kg, 3 mg if 60–70 kg, 4 mg if 70 kg+), with intravenous saline as placebo (1 ml). Additional midazolam was titrated if initial sedation was inadequate.

Group A received intravenous alfentanil ($0{\cdot}5\ mg\ ml^{-1}$) with intravenous saline as placebo (dose titrated according to weight as if midazolam). Additional alfentanil was titrated if initial sedation was inadequate (0·25 mg aliquots).

Group M+A received intravenous alfentanil ($0{\cdot}5\ mg\ ml^{-1}$), intravenous midazolam (dose titrated according to weight) with additional midazolam if initial sedation was inadequate.

All patients therefore received two injections; either saline placebo and active drug or two active drugs. The syringes were made up by one unblinded author. Two authors only gave the sedation remaining blind and performed all bronchoscopies.

All drugs were injected slowly through an intravenous cannula, Venflon (Viggo Spectromed) which remained *in situ* during the bronchoscopy. All patients also received intravenous atropine (0·6 mg), and lignocaine 4% (1 ml) via transcricoid membrane injection, and (1 ml) through the bronchoscope once in the trachea. Additional aliquots of lignocaine 2% (2 ml) were given through the bronchoscope

0954-6111/95/010053+04 $08.00/0

Table 1

	M	M+A	A
Number	34	33	35
Sedation			
Midazolam	Average 5·7 mg Range 2–10 mg	Average 4·5 mg Range 2–10 mg	—
Alfentamil	—	0·5 mg	Average 0·66 mg Range 0·05–1 mg
Duration of procedure (from insertion of bronchoscope to removal)	Average 5·5 min Range 5–15 min	Average 7·5 min Range 2–19 min	Average 5·9 min Range 1·5–12 min

during the procedure for troublesome coughing. Full resuscitation equipment was available in the bronchoscopy suite, along with the antidotes, flumazenil and naloxone to counteract both sedatives. Oxygen was available and oxygen saturation measured by a pulse oximeter (Satlite Trans. Dantex) which was attached to an index finger.

The duration of the procedure, number of coughs and extra aliquots of lignocaine required for each patient were recorded by one independent observer. After the procedure the level of discomfort experienced as perceived by both patient and bronchoscopist was charted on a 10 cm visual analogue scale. This was then expressed as a percentage with 100% score equal to no discomfort.

The recovery time was assessed by the ability of the patient to obey some simple commands (e.g. open eyes or mouth).

Comparisons were made for each measurement between the three groups, i.e. Group M, Group A and Group M+A. As the parameters measured were not normally distributed, all comparisons were made using the Mann–Whitney U-test.

The study was given approval by the Hospital Ethics Committee.

Results

One hundred and three patients were randomized: 34 randomized to Group M, 35 to Group A and 33 to Group M+A. The amount of sedation given to each group is shown in Table 1.

There were significantly fewer coughs min^{-1} in Group A compared with Group M ($P=0{\cdot}0053$) and Group M required more additional aliquots of lignocaine compared with Group A ($P<0{\cdot}005$) and Group M+A ($P<0{\cdot}002$).

The oxygen saturation fell significantly more in Group M+A compared with Group A ($P=0{\cdot}0037$) and appeared to fall more in Group M+A compared with Group M though not to a significant degree. There was no significant difference between the bronchoscopist or patient's perception of discomfort between the three groups (Table 2).

Recovery time was immediate, all patients being able to respond to simple commands at the end of the procedure and were able to return home within 2 h.

Discussion

Fibre optic bronchoscopy is now routinely performed as an outpatient procedure. It is therefore important that sedation is optimal with good anxiolytic, amnesic and anti-tussive qualities and of short duration of action. From the bronchoscopist's point of view, control of coughing is particularly important as this facilitates ease of viewing the bronchial tree and of obtaining good biopsy material.

Midazolam and alfentanil were selected for this study as both appeared to meet the above criteria. Midazolam is a sedative drug with amnesic qualities which has a rapid 2 h half-life and is metabolized to inactive products, unlike diazepam which is metabolized to desmethyldiazepam prolonging its action. Alfentanil is an opioid and therefore has theoretical anti-tussive action. It is a synthetic derivative of fentanyl which is 5–10 times less potent than fentanyl. It has a very short duration of action with peak effect in 90 s and duration of action only 5–10 min (onset of action four times more rapid and a third the duration of fentanyl). There is however the risk of dose-related respiratory depression and occasional unpredictable effects have been noted so patients should be observed for 2 h post dose.

Alfentanil proved to have significantly better anti-tussive qualities than midazolam as shown by both the reduced cough count and reduced lignocaine requirements. There was a trend for the bronchoscopist to perceive the patient to be more comfortable with alfentanil, presumably due to the fact that they

Table 2

	M	M+A	A	Significance
Coughs min^{-1}	2·45 ± 1·67	1·72 ± 1·28	1·42 ± 1·67	MvA $P=0·0053$
Lignocaine (No. of aliquots) Additional	0·79 ± 0·6	0·34 ± 0·59	0·37 ± 0·55	AvM $P<0·005$ M+AvM $P<0·002$
Visual Analogue Score (bronchoscopist)	54·5% ± 30·9	72·9% ± 26·3	79·9% ± 19·8	NS
Visual Analogue Score (patient)	88·2% ± 13·6	86% ± 24·9	72% ± 32·7	NS
Minimum % drop in O_2 saturation	9·6% ± 4·5	13·5% ± 9·1	8·6% ± 6·2	M+AvA $P=0·033$ MvA NS M+AvM NS

coughed less making the procedure easier. One would have expected the patients who received midazolam to have reported less discomfort due to its amnesic qualities. There appeared to be a slight trend in this direction but not as pronounced as the trend of the bronchoscopist's perception of the patient's discomfort.

There have been numerous previous studies comparing a variety of sedative regimes. Simpson's postal study of bronchoscopic practice (1) revealed that 40% of doctors in the U.K. used a benzodiazepine and 20% use a combination of opiate and benzodiazepine, but evidence for the effectiveness of the different combinations is confusing. Diazepam has been compared to morphine as premedication for gastroscopy (4), diazepam being preferred because of increased sedation and amnesia, although the degree of cooperation of patients was not significantly different between the groups. Numerous studies have compared midazolam with diazepam (5–9) and in most cases, midazolam was preferred, usually because of greater amnesic effect. Some authors felt drowsiness was excessive but in these cases very large doses of midazolam (up to 20 mg) were used. Diazepam and fentanyl in combination were thought to be more effective than papaveretum and hyoscine (10), but all measurements were based on a questionnaire completed by patients and no objective parameters were studied. Two studies have considered anti-tussive qualities. Temazepam was compared with papaveretum (11) but no formal measurements were recorded, doctors merely giving a subjective assessment of the frequency of coughing following the procedure. There was no significant difference between the two drugs. A more useful study compared relatively light sedation with alfentanil with the deeper sedation of papaveretum combined with diazepam (12). A significant reduction in cough count was noted in the alfentanyl group, whilst as in this study, there was no significant difference in the level of discomfort as assessed by patients using a visual analogue scale between the two groups.

The safety of any sedation is of paramount importance. A postal study (1) showed nationwide mortality due to fibre optic bronchoscopy to be 0·04% and incidence of major complications to be 0·12% (i.e. 44 from 34 462 of which 12 patients had respiratory depression). In our study, all patients desaturated as expected during routine bronchoscopy. It has been shown that fibre optic bronchoscopy alone can result in a fall of P_aO_2 by up to 21 mmHg (13). Those who received the combination of midazolam and alfentanil had a significantly greater drop in oxygen saturation when compared with each drug given singly. There was no significant difference in the fall of oxygen saturation between the midazolam and alfentanil groups alone and it is likely that the fall in oxygen saturation with the combination (M+A) was due to a larger total dose of sedative drugs.

Since one of the aims of this study was to assess the effect of sedation on oxygen saturation, oxygen was not routinely given despite marked desaturation in some patients, although oxygen was always available. It is now our practice to monitor all procedures with pulse oximetry and provide supplemental oxygen via a nasal cannula to patients who desaturate.

In conclusion this study confirms previous findings that alfentanil provides adequate sedation for outpatient fibre optic bronchoscopy while combining more effective anti-tussive effects than midazolam.

The combination of alfentanil and midazolam does not provide significantly better sedation in terms of patients perceived discomfort, at a cost of greater risk of oxygen desaturation due to the larger total dose of sedation.

Finally, despite the apparent good safety profile of the alfentanil, we still feel that fibre optic bronchoscopy should be carried out in the presence of full resuscitative equipment, including antidotes.

References

1. Simpson FG, Arnold AG, Purvis A, Belfield PW, Muers MF, Cooke NJ. Postal survey of bronchoscopic practice by physicians in the U.K. *Thorax* 1986; **41:** 311–317.
2. Rees PJ, Hay JG, Webb JR. Premedication for fibreoptic bronchoscopy. *Thorax* 1983; **38:** 624–627.
3. Shelley MP, Wilson P, Norman J. Editorial: sedation for fibreoptic bronchoscopy. *Thorax* 1989; **44:** 769–775.
4. Ludlam R, Bennett JR. Comparison of diazepam and morphine as premedication for gastrointestinal endoscopy. *Lancet* 1971; **ii:** 1387–1399.
5. Berggren L, Eriksson I, Mollersholt P, Wickbom G. Sedation for fibreoptic gastroscopy: a comparative study of midazolam and diazepam. *Br J Anaesth* 1983; **55:** 289–296.
6. Boldy DAR, Lever LR, Unwin PR, Spencer PA, Hoare AM. Sedation for endoscopy: midazolam or diazepam and pethidine? *Br J Anaesth* 1988; **61:** 698–701.
7. Korttila E, Tarkkanen J. Comparison of diazepam and midazolam for sedation during local anaesthesia for bronchoscopy. *Br J Anaesth* 1983; **57:** 581–586.
8. Magni VC, Frost RA, Leung JWC, Cotton PB. A randomized comparison of midazolam and diazepam for sedation in upper gastrointestinal endoscopy. *Br J Anaesth* 1983; **55:** 1095–1101.
9. Whitham JG, Al-Khudhairi D, McCloy RF. Comparison of midazolam and diazepam in doses of comparable potency during gastroscopy. *Br J Anaesth* 1983; **55:** 773–777.
10. Goroszeniuk T, Nicholas IH, Marchant P, Turner JA McM, Johnson N McI. Premedication for fibreoptic bronchoscopy: fentanyl, diazepam and atropine compared with papavertum and hyoscine. *BMJ* 1980; **281:** 486.
11. Dorward AJ, Berkin KE, Elliott JA, Stack BHR. A double-blind controlled study comparing temazepam with papavertum as premedication for fibreoptic bronchoscopy. *Br J Dis Chest* 1983; **77:** 60–65.
12. Webb AR, Doherty SF, Chester MR *et al.* Sedation for fibreoptic bronchoscopy: comparison of alfentanil with papaveretum and diazepam. *Resp Med* 1989; **83:** 213–217.
13. Dubrowsky C, Awe RT, Jenkins DE. The effect of bronchofibreoscopic examination oxygenation status. *Chest* 1975; **67:** 137–140.