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Propofol *versus* combined sedation in flexible bronchoscopy: a randomised non-inferiority trial

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ABSTRACT: Combined sedation with a benzodiazepine and an opiate has been proposed as standard sedation for bronchoscopy. Propofol is a sedative–hypnotic with a rapid onset of action and fast recovery time, but carries the potential risk of respiratory failure.

Consecutive patients (n=200) were randomly allocated to receive either the combination midazolam and hydrocodone or intravenous propofol. The primary end-points were the mean lowest arterial oxygen saturation during bronchoscopy and the readiness-for-discharge score 1 h after the procedure.

The mean lowest arterial oxygen saturation during bronchoscopy did not differ across treatment groups (p=0.422), and the number of patients recording an arterial oxygen saturation of ⩽90% on at least one occasion was similar in both groups (p=0.273). The median (interquartile range) readiness-for-discharge score 1 h after the procedure was significantly higher in the propofol group than in the combined sedation group (8 (6–9) *versus* 7 (5–9); p=0.035). Patients assigned propofol exhibited less tachycardia during bronchoscopy and for ⩾1 h after the examination. Minor procedural complications were noted in 71 (35.5%) patients and exhibited a similar incidence in both treatment arms (p=0.460).

Propofol is as effective and safe as combined sedation in patients undergoing flexible bronchoscopy, thus representing an appealing option if timely discharge is a priority.

KEYWORDS: Analgesia, endoscopy, lung, pre-medication, procedure

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The current guidelines for bronchoscopy recommend offering sedation to all patients undergoing flexible bronchoscopy, except where there are contraindications [1]. The aim of sedation is to achieve good patient tolerance, comfort and cooperation whilst reducing complications of the procedure [2–4]. A recent European survey has shown that >95% of centres routinely perform sedated bronchoscopy [5].

Although the ideal sedation for flexible bronchoscopy is not yet defined [1], the combination of a benzodiazepine and an opiate has been shown to improve operating conditions due to its antitussive effect, enhance patient satisfaction and be safe [6]. Thus combined sedation using a benzodiazepine and an opiate has been proposed for adoption as standard sedation for patients without contraindications [7, 8]. In such patients, midazolam is the most commonly used benzodiazepine because of its short duration of action [5]. However, the pharmacokinetic properties of midazolam include a significant variation in individual dose requirements and delayed metabolism, leading to accumulation of the drug in ~6% of the population [9, 10]. Both attributes may lead to a prolonged recovery period [11–14]. This has important implications for a busy day-case service, including decreased patient throughput, less efficient use of day-care beds and increased staff-costs.

Propofol (2,6-diisopropylphenol) is a sedative–hypnotic frequently used in the induction and maintenance of anaesthesia [15]. Its rapid onset of action and amnesic properties, coupled with smooth and rapid recovery, make propofol an appealing agent for procedural sedation [16, 17]. The significant advantage of a faster recovery time, as compared to other sedatives, has been emphasised in several studies [9, 18–20]. However, to date, there are only limited data evaluating propofol for flexible bronchoscopy and no safety data comparing propofol with combined sedation in this setting. Therefore, a prospective randomised non-inferiority trial was undertaken in order to determine whether

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propofol is as effective and safe as combined sedation with a benzodiazepine and an opiate in patients undergoing flexible bronchoscopy. The primary end-points were the mean lowest arterial oxygen saturation during bronchoscopy and the readiness-for-discharge score 1 h after the procedure.

METHODS

Patients

Consecutive patients (n=200) undergoing elective flexible bronchoscopy were randomly allocated to receive either intravenous propofol or the combination midazolam and hydrocodone as sedative agent. Intubated patients and those with known allergy or intolerance to midazolam, hydrocodone or propofol were not included in the study. Informed consent was obtained from each patient, and the study was approved by the institutional review board, Ethikkommission beider Basel (Basle, Switzerland). The trial was registered with the Current Controlled Trials database (trial number ISRCTN99754241) [21].

Study design

All patients were assessed by a physician and a member of the nursing team trained in anaesthesiology prior to the procedure, which included gradation of physical status in accordance with the American Society of Anaesthesiologists (ASA) criteria and estimation of the Mallampati score. Bronchoscopy procedures were performed transnasally, with the patients in the semi-recumbent position, by a total of four pulmonary fellow physicians under the close supervision of four pulmonary attending physicians. Pulse oximetric results were recorded continuously during the procedure and automated noninvasive blood pressure monitoring was performed every 5 min. Supplemental oxygen was offered at 4 $L \cdot min^{-1}$ *via* a nasal cannula to all patients. In the case of desaturation to $\leqslant$90%, oxygen delivery was increased to 6 $L \cdot min^{-1}$ [22]. Nasal anaesthesia was achieved by spraying 10% lidocaine in the nasopharynx (four times) and oropharynx (twice). Bronchoscopists were advised to instil 3-mL aliquots of 1% lidocaine over the vocal cords and on to the trachea and both right and left main bronchi. Instilled lidocaine doses were recorded for each patient. All doses of supplemental local anaesthesia required, as judged by the bronchoscopist, were recorded for each patient. No inhaled lidocaine was given prior to the procedure [7].

Patients were randomly assigned to either intravenous propofol or the combination of midazolam and hydrocodone. Every patient's assignment was carried out in the waiting room of the bronchoscopy suite by a research nurse. Randomisation was through arbitrary allocation to one of the two treatment groups based on a computer-generated random list (GraphPad Software, San Diego, CA, USA).

The loading doses of propofol and midazolam were titrated in order to achieve adequate conscious sedation (onset of ptosis for bronchoscopy). Patients assigned the combination of midazolam and hydrocodone received 5 mg intravenous hydrocodone immediately before flexible bronchoscopy [6]. Thereafter, conscious sedation was achieved initially with 2 mg midazolam and followed by further 1–2 mg intravenous midazolam boluses during the procedure at the endoscopist's discretion [6]. The dose of midazolam during the procedure was titrated to maintain conscious sedation, *i.e.* induce an altered state of consciousness that minimises pain and discomfort but still permits a patient to respond to physical stimulation and maintain an unassisted airway. Patients assigned propofol received an intravenous infusion using an intermittent bolus technique; after an initial 20 mg intravenous propofol, the dose was then carefully titrated. For ASA I and II patients, the steps comprised 10–20 mg intravenous propofol, whereas, for ASA III and IV, exactly 10 mg intravenous propofol was administered based on the clinical response, as previously described [23]. Between each bolus, a pause lasting $\geqslant$20 s had to be observed. If the effect disappeared during the examination, additional intravenous boluses of 10 mg propofol were given, depending on the clinical effect, in order to maintain the required level of sedation. Signs of pain or discomfort, agitation, persistent cough, and inadequate motor or verbal response to manipulation were considered indicators of insufficient sedation, leading to administration of an additional dose of propofol (10–20 mg) or midazolam (1–2 mg). The total dose of propofol and midazolam was documented for each patient.

Diagnostic procedures, *i.e.* brushing, washings, biopsy, bronchoalveolar lavage, and endobronchial and transbronchial biopsy, were performed dependent upon the clinical indication. Haemodynamic parameters, sedation, duration of bronchoscopy, bronchoscopic procedures and complications were noted during the procedure on a form specifically designed for the study. Complications were defined as oxygen desaturation of $\leqslant$90%, need for mandible support, minor and major bleeding, arterial hypotension, need for artificial airway or invasive ventilation, need to abort bronchoscopy, need for intensive care unit (ICU)/intermediate care stay, pneumothorax and death.

At the end of the procedure, bronchoscopists and nursing staff charted their perception of cough during the procedure on a 10-cm visual analogue scale (VAS). Similarly, 2 h after bronchoscopy, patients were also asked to record their perception of cough related to the procedure on a 10-cm VAS. On this scale, 0 denoted no cough and 10 represented incessant cough. Patients were also asked to record fear and discomfort associated with the procedure on a 10-cm VAS. On this scale, 0 denoted no fear or discomfort and 10 represented the greatest thinkable fear or discomfort. After 1 and 2 h, respectively, patients were asked about their readiness for discharge. On the VAS, 0 denoted no readiness for discharge and 10 represented immediate readiness for discharge. Willingness to undergo repeat flexible bronchoscopy was also documented. Haemodynamic monitoring was performed immediately before, during and shortly after the procedure (after removal of the bronchoscope), and before transfer from the bronchoscopy suite to the recovery room. Moreover, the patient's blood pressure and cardiac frequency were monitored for up to 3 h after bronchoscopy until discharge.

Data analysis

Assuming a mean lowest arterial oxygen saturation of 94.8% with an SD of 2.7% in the arm treated with the combination of midazolam and hydrocodone [6], a total of 174 patients, 87 in each treatment arm, would be needed to demonstrate that propofol is associated with a mean lowest saturation within 2% or better of that of the combination of midazolam and hydrocodone, with 90% power using a one-sided statistical

test with an α of 0.05. Assuming a 10% loss to follow-up, a sample size of 200 patients was projected.

The difference in arterial oxygen saturation change between the randomised groups, taking into account the initial arterial oxygen saturation, was analysed using a general linear model of repeated measures. Differences in dichotomous variables were evaluated using the Chi-squared test or Fisher's exact test, as appropriate. Normally distributed parameters were analysed using an unpaired t-test for equality of means. All other continuously non-normally distributed parameters were evaluated using the nonparametric Mann–Whitney U-test or Kruskal–Wallis test, as appropriate. Correlation analyses between physicians and nursing staff VAS results were performed using Spearman rank correlation.

The Statistical Package for Social Sciences (SSPS, Inc.) version 15 for Windows program (SPSS, Chicago, IL, USA) was used. All test were two-tailed; a p-value of <0.05 was considered significant. Results are expressed as mean$\pm$SD or median (interquartile range) unless otherwise stated.

RESULTS

Patient demographics are presented in table 1. There were no significant differences between the two randomised groups in terms of age, presence of comorbid conditions, physical status or Mallampati score.

Table 2 shows the indication, number and distribution of diagnostic procedures per patient, and randomisation group. The main reason for bronchoscopy was pulmonary infection, followed by suspicion of malignancy and interstitial lung disease. Accordingly, the most common diagnostic procedures were bronchoalveolar lavage (58%) and bronchial washing (33%). Transbronchial needle aspiration, both from the mediastinum and the periphery of the lung, was performed in 30.5% of cases. The great majority of patients underwent two (39%) or three (35.5%) diagnostic bronchoscopic procedures. The mean$\pm$SD midazolam dose required was 8$\pm$3.5 mg and the propofol dose required was 217$\pm$131 mg.

Primary end-points

Mean lowest arterial oxygen saturation during the procedure

The mean lowest arterial oxygen saturation during the procedure was similar across treatment groups (p=0.422) (fig. 1). Correspondingly, there was no significant difference in the arterial oxygen saturation change from baseline through re-evaluation between patients randomised to the combination of midazolam and hydrocodone and those randomised to propofol (p=0.644) (fig. 2). The number of patients who recorded a saturation of $\leqslant$90% on at least one occasion was also similar in both groups (25 midazolam/hydrocodone *versus* 32 propofol; p=0.273). The median (interquartile range) maximum oxygen requirement during the procedure did not differ between patients treated with midazolam and hydrocodone (4 (4–8) L) and those treated with propofol (4 (4–8) L; p=0.081).

Readiness-for-discharge score an hour after the procedure

The median (interquartile range) readiness-for-discharge score 1 h after the procedure was 7 [5–9] in patients sedated with the combination of midazolam and hydrocodone and 8 [6–9] in patients sedated with propofol (p=0.035). An hour after the procedure, a readiness-for-discharge score of $\geqslant$6 was noted in 59 patients treated with the combination midazolam and hydrocodone and in 75 patients treated with propofol (p=0.003). A total of 17 patients were unable to answer any question at the re-evaluation 1 h after the procedure (16 midazolam/hydrocodone *versus* 1 propofol; p<0.001). Eight patients were still drowsy and unable to speak 2 h after the procedure (seven midazolam/hydrocodone *versus* one propofol; p=0.030).

Secondary end-points

The haemodynamic findings before, during and after bronchoscopy are shown in table 3.

As compared to combined sedation with midazolam and hydrocodone, patients assigned propofol exhibited less tachycardia during bronchoscopy, and this difference in cardiac frequency was significant for $\geqslant$1 h after the procedure. Systolic blood pressure was higher at the end of bronchoscopy in patients sedated with the combination midazolam and hydrocodone (p=0.002).

Procedural complications were noted in 71 (35.5%) patients and exhibited a similar incidence in both treatment arms (p=0.460) (fig. 3). The most common complications were the need for chin support (n=68; 34%) and an arterial oxygen saturation of $\leqslant$90% (n=57; 28.5%). A nasopharyngeal tube was

TABLE 1 Baseline characteristics of 200 consecutive patients undergoing flexible bronchoscopy

	Midazolam/ hydrocodone	Propofol	p-value
Subjects n	100	100	
Age yrs	61.6 (21–87)	61.0 (23–89)	0.895
Male sex	65 (65)	62 (62)	0.659
Height cm	170.6$\pm$8.6	171.3$\pm$9.5	0.853
Weight kg	76.0$\pm$17.1	73.9$\pm$16.4	0.323
Current smoker	28 (28)	30 (30)	0.876
Ex-smoker	42 (42)	41 (41)	0.886
Smoking history pack-yrs	31.1$\pm$33.2	27.1$\pm$27.1	0.396
Comorbid conditions			
Malignancy	35 (35)	33 (33)	0.765
COPD	25 (25)	25 (25)	1.000
Immunosuppression	25 (25)	16 (16)	0.115
Cardiopathy	20 (20)	13 (13)	0.182
Renal failure	4 (4)	5 (5)	0.733
Stroke	3 (3)	3 (3)	1.000
Alcoholism	2 (2)	3 (3)	0.651
Platelets 10^9 g·L^{-1}	308$\pm$169	295$\pm$144	0.641
ASA physical status	3 (2–3)	3 (2–3)	0.777
Mallampati score	2 (2–3)	2 (2–3)	0.355

Data are presented as mean$\pm$SD, mean (range) for age, median (interquartile range) for ASA physical status and Mallampati score, or n (%), unless otherwise indicated. COPD: chronic obstructive pulmonary disease; ASA: American Society of Anesthesiologists.

TABLE 2 Indication for examination, number and distribution of diagnostic procedures per patient, and randomisation group in 200 patients undergoing flexible bronchoscopy

	Midazolam/ hydrocodone	Propofol	Total	p-value
Subjects n	100	100	200	
Indication				
Infection	38 (38)	28 (28)	66 (33)	0.133
Suspicion of malignancy	31 (31)	31 (31)	62 (31)	1.000
Interstitial lung disease	13 (13)	12 (12)	25 (12.5)	0.831
Pre/post-interventional	6 (6)	7 (7)	13 (6.5)	0.774
Haemoptysis	3 (3)	5 (5)	8 (4)	0.721
Chronic cough	2 (2)	2 (2)	4 (2)	1.000
Bronchial toilette	1 (1)	2 (2)	3 (1.5)	1.000
Miscellaneous	6 (6)	13 (13)	19 (9.5)	0.099
Diagnostic procedures				
Bronchial washings	28 (28)	38 (38)	66 (33)	0.133
Bronchial brushing	18 (18)	13 (13)	31 (15.5)	0.329
Endobronchial biopsy	17 (17)	18 (18)	35 (17.5)	0.852
Transbronchial biopsy	24 (24)	22 (22)	46 (23)	0.737
Bronchoalveolar lavage	62 (62)	54 (54)	116 (58)	0.252
TBNA mediastinum	27 (27)	19 (19)	46 (23)	0.179
TBNA periphery	8 (8)	7 (7)	15 (7.5)	0.788
EBUS	3 (3)	5 (5)	8 (4)	0.470
Procedures per patient				
Inspection alone	4 (4)	4 (4)	8 (4)	1.000
Two	36 (36)	42 (42)	78 (39)	0.469
Three	37 (37)	34 (34)	71 (35.5)	0.383
Four	17 (17)	15 (15)	32 (16)	0.705
Five	4 (4)	4 (4)	8 (4)	1.000
Six	2 (2)	1 (1)	3 (1.5)	1.000

Data are presented as n (%), unless otherwise indicated. TBNA: transbronchial needle aspiration; EBUS: endobronchial ultrasonography.

required in three cases; one patient was transferred to the ICU. There were no deaths.

The median (interquartile range) duration of the procedure was similar in patients receiving midazolam and hydrocodone (17 (10–24) min) and in those receiving propofol (17 (9–28) min; p=0.941) (table 4). There was also no difference in the required dose of lidocaine in the two randomised groups (p=0.926). Cough scores, as judged by the bronchoscopists and nursing staff, did not differ between patients randomised to combined sedation and propofol. Conversely, cough scores, as judged by patients themselves, were significantly lower in the group treated with combined sedation than with propofol. There was no difference in the discomfort related to the procedure across treatment groups (p=0.162).

Arterial carbon dioxide tension (P_{a,CO_2}) was assessed in 42 (84%) out of the 50 patients with chronic obstructive pulmonary disease before the procedure. In these patients, the mean±SD forced expiratory volume in 1 s was 1.54±0.67 L and 56±19% of the predicted value. The mean P_{a,CO_2} was 40.2±4.9 mmHg. Hypercapnic status, as defined by a P_{a,CO_2} of ⩾45 mmHg on arterial blood gas analysis, was evidenced in five cases. In hypercapnic patients, chin support was required in three cases, and arterial oxygen saturation of ⩽90% was documented in two cases during the procedure. These figures did not differ significantly from those observed in normocapnic patients (p=0.716 and p=0.891, respectively).

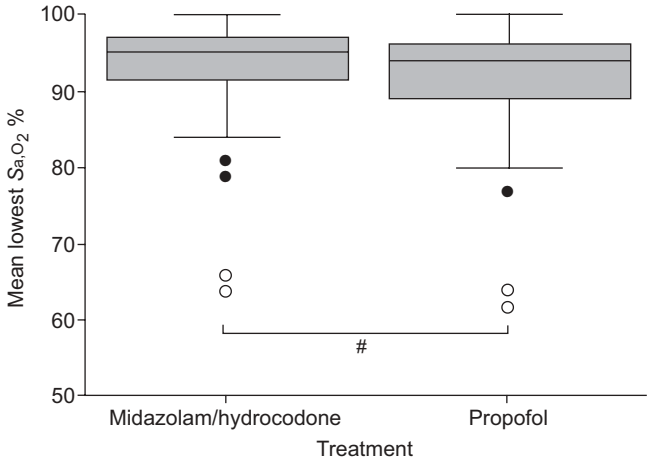

FIGURE 1. Mean lowest arterial oxygen saturation (S_{a,O_2}) during bronchoscopy in the two patient groups. Boxes represent median and interquartile range; whiskers represent range. ●: outliers; ○: extreme outliers. #: p=0.422.

DISCUSSION

The present study has demonstrated that the mean lowest arterial oxygen saturation and number of procedural complications are similar in patients receiving the combination midazolam and hydrocodone and those receiving propofol for sedation during flexible bronchoscopy. Herein, operating conditions, as assessed by duration of the procedure or need for supplemental lidocaine, were also comparable. Therefore, propofol is a valid alternative to combined sedation with a benzodiazepine and an opiate. The use of propofol was associated with a significantly higher readiness-for-discharge score 1 h after the examination and a lower proportion of persistent sedation 2 h after bronchoscopy, whereas the use of combined sedation was associated with lower cough scores as assessed by patients. Hence, both drugs regimens have peculiar sedating characteristics and the choice of one over the other might rely on the preferences of the patient and bronchoscopist, as well as on infrastructural circumstances, *e.g.* expected time to discharge.

To the present authors' knowledge, this is the first randomised controlled non-inferiority trial comparing propofol with the combination of a short-acting benzodiazepine and an opiate as a sedative agent during flexible bronchoscopy. The combination of a short-acting benzodiazepine and an opiate has been shown to improve operating conditions due to its antitussive effects and to improve patient satisfaction. Thus it has been suggested that combined sedation be adopted as standard sedation for patients without contraindications, particularly if diagnostic bronchoscopic procedures, *e.g.* transbronchial biopsy, are performed [6, 7]. Former studies on propofol were performed utilising a benzodiazepine alone or a long-acting benzodiazepine [24–26]. RANDELL [26] showed a significantly lower respiratory frequency in patients receiving the combination

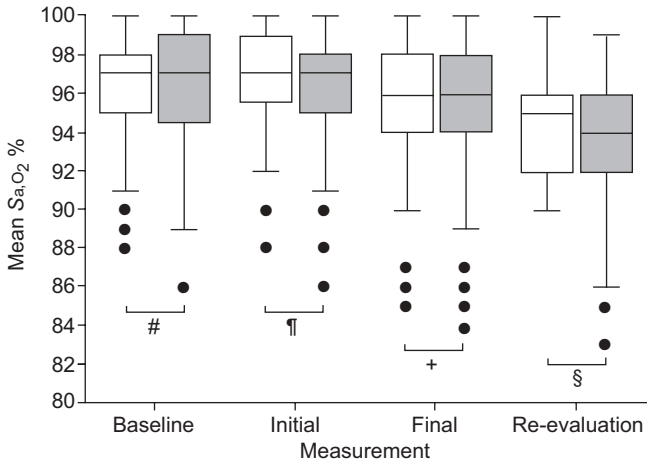

FIGURE 2. Mean arterial oxygen saturation (Sa,O_2) with midazolam/hydrocodone (□) and propofol (■) at baseline, at the beginning of the procedure (Initial), at the end of the procedure (Final) and on re-evaluation after 1 h. Boxes represent median and interquartile range; whiskers represent range. ●: outliers. There was no significant difference in the Sa,O_2 change with time across groups (p=0.644). #: p=0.625; ¶: p=0.436; +: p=0.653; §: p=0.481.

diazepam and fentanyl as compared to propofol alone. However, midazolam has replaced diazepam in most centres due to its shorter duration of action compared to diazepam, and is now by far the most common sedative used during bronchoscopy [1, 5].

CRAWFORD *et al.* [25] compared sedation for flexible bronchoscopy provided by incremental doses of midazolam alone with that provided by a computer-controlled infusion of propofol. Operator and patient acceptability, anxiolysis, and the effect on systolic arterial pressure did not differ between the groups. Conversely, arterial oxygen saturation during the procedure fell more in those who received propofol than in those who received midazolam (83% in the propofol group and 86% in the midazolam group). It is well known that both propofol and midazolam may produce respiratory depression [25, 27]. Contrary to the current British Thoracic Society recommendations, oxygen supplementation was not routinely provided in that study. Supplemental oxygen is routinely given to all patients undergoing flexible bronchoscopy at most institutions [1, 28]. The present randomised trial showed that, if supplemental oxygen is routinely provided during bronchoscopy, propofol does not cause a greater fall in arterial oxygen saturation than does the combination of midazolam and hydrocodone.

KESTIN *et al.* [24] examined the cardiovascular stability and rate of recovery in patients receiving propofol infusions with or without alfentanil for rigid oesophagoscopy and/or bronchoscopy. All patients received a neuromuscular blocker during induction of anaesthesia and were intubated for the endoscopic procedure. The authors found no difference in haemodynamic parameters, recovery time or adverse events in the two groups, but patients receiving propofol combined with alfentanil required a mean lower dose of propofol during the procedure. Since all patients were intubated for the examination, this study does not permit any inferences about safety in non-intubated patients undergoing routine flexible bronchoscopy. Nevertheless, it is tempting to speculate that the combination of propofol and hydrocodone could reduce the total propofol dose required during flexible bronchoscopy.

TABLE 3 Haemodynamic findings before, during and after bronchoscopy in patients randomised to sedation with the combination of midazolam and hydrocodone and propofol

Measurement	Midazolam/ hydrocodone	Propofol	p-value
Subjects n	100	100	
Baseline			
Systolic BP mmHg	138±22	134±24	0.105
Diastolic BP mmHg	79±17	80±15	0.713
Cardiac frequency beats·min^{-1}	83±14	83±16	0.816
Initial			
Systolic BP mmHg	133±26	128±23	0.060
Diastolic BP mmHg	80±16	78±16	0.192
Cardiac frequency beats·min^{-1}	88±15	83±15	**0.040**
Final			
Systolic BP mmHg	135±24	125±26	**0.002**
Diastolic BP mmHg	78±15	73±23	0.098
Cardiac frequency beats·min^{-1}	91±16	87±15	**0.013**
Re-evaluation after 1 h			
Systolic BP mmHg	122±20	122±22	0.832
Diastolic BP mmHg	71±14	71±17	0.993
Cardiac frequency beats·min^{-1}	90±14	85±17	**0.040**
Re-evaluation after 2 h			
Systolic BP mmHg	131±20	129±18	0.906
Diastolic BP mmHg	78±11	76±11	0.288
Cardiac frequency beats·min^{-1}	84±13	83±14	0.469

Data are presented as mean± SD, unless otherwise indicated. BP: blood pressure. Values in bold show statistical significance.

Although both drugs performed equally well with regard to safety in the present study, we found significant differences between the two groups in post-operational VAS readiness-for-discharge score and the number of patients showing signs of persistent sedation 2 h after the procedure. These findings are in accordance with previous data suggesting that midazolam causes significant impairment of memory and motor reactions 60 min after the end of the procedure [9, 25]. Accordingly, central nervous system impairment may persist for $\geqslant$3.5 h after antagonism of midazolam sedation with flumazenil, although patients may have a subjective feeling of alertness, which might have dangerous consequences [29].

Considering the mean doses required in the present study, sedation with propofol was five times more expensive than sedation with the combination of midazolam and hydrocodone (mean cost 15.66±9.46 *versus* 2.92±0.18 Euros, respectively). Nevertheless, the costs related to sedative medication represent only a small percentage of the overall cost of bronchoscopy. Although figures may vary markedly across countries, continuous peri-interventional monitoring generates up to a third of the procedure cost in Switzerland. Prolonged sedation may prevent discharge, thus disrupting a tight schedule and

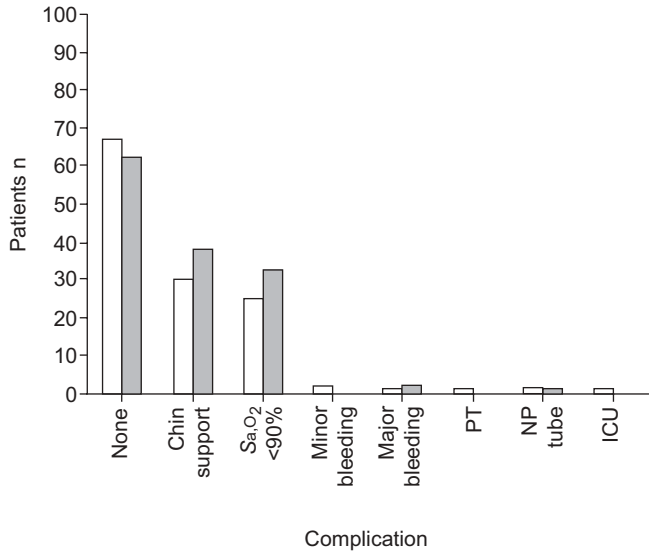

FIGURE 3. Complications of bronchoscopy in patients assigned the combination midazolam and hydrocodone (□; n=100) and propofol (■; n=100). Sa,O_2: arterial oxygen saturation; PT: pneumothorax; NP: nasopharyngeal; ICU: intensive care unit.

increasing procedural costs. Therefore, having proved that propofol is as effective and safe as standard combined sedation with a benzodiazepine and an opiate, the present data suggest that propofol might be an appealing option if timely discharge is a priority for either the patient or medical staff.

Interestingly, cough scores, as judged by the patients themselves, were significantly lower in the group treated with combined sedation than that treated with propofol. In contrast, cough scores, as judged by the bronchoscopists and nursing staff, did not differ between the randomised groups. We hypothesise that these findings can be explained by the amnesic effect of midazolam. According to several previous studies, the wake-up time for combined sedation with an opiate and a benzodiazepine is 35–60 min and discharge time 75–120 min after the procedure [30–32]. Alternatively, propofol might have a shorter or less potent effect on the cough reflex than the combination of midazolam and hydrocodone [33, 34].

The incidence of adverse events in the present study was similar to that described in previous reports [9, 35]. It is worth noting that it is now appreciated that oxygen desaturation during invasive endoscopic procedures is a common phenomenon, both with [9, 35] and without oxygen supplementation [31]. This observation emphasises the importance of standard pulse oximetry and oxygen supplementation during flexible bronchoscopy, as stated in the British Thoracic Society guidelines [1]. Additionally, particular care should be taken in patients at higher risk of carbon dioxide retention during bronchoscopy [1]. Pre-operative arterial blood gas assessment is usually required in such patients. Although the present data do not demonstrate an obviously increased risk of propofol sedation in hypercapnic patients, monitoring of transcutaneous carbon dioxide may be useful in avoiding the complications related to any kind of sedation in these high-risk patients [36].

TABLE 4 Outcome parameters in patients randomised to sedation with the combination of midazolam and hydrocodone and propofol

	Midazolam/ hydrocodone	Propofol	p-value
Subjects n	100	100	
Duration of the procedure min	17 (10–24)	17 (9–28)	0.941
Lidocaine dose mg	132±40	136±44	0.926
Cough score VAS			
Physician	4 (2–6)	5 (2–7)	0.781
Nurse	4 (2–7)	5 (3–7)	0.489
Patient	0 (0–3)	2 (0–6)	**<0.001**
Discomfort score (patient) VAS	0 (0–0)	0 (0–0)	0.162
Fear VAS			
Today's bronchoscopy	0 (0–2)	0 (0–3)	0.151
Future bronchoscopy	0 (0–0)	0 (0–0)	**<0.007**
Readiness for discharge VAS			
After 1 h	7 (5–9)	8 (6–9)	**0.035**
After 2 h	9 (7–10)	9 (7–10)	0.131

Data are presented as mean± SD or median (interquartile range), unless otherwise indicated. VAS: visual analogue scale. Values in bold show statistical significance.

The present study has a few limitations. We used a standardised VAS score, a subjective tool, for assessing readiness for discharge following bronchoscopy. Taking into account that the short half-life of propofol is well described [9], we believe that it was fair to apply a clinical tool for appraising discharge suitability. Thus we refrained from performing formal measurements of motor and verbal function. Further, this was not a blinded study and the specific macroscopic characteristics of propofol facilitate its identification. In this context, concerns regarding potential drops in arterial oxygen saturation might have resulted in a less-than-optimal dose in those patients allocated to the propofol arm. This might be the reason why patients treated with propofol showed higher cough scores (judged by the patients themselves). Another factor to consider is that the nursing staff of Basle University Hospital (Basle, Switzerland) have considerable expertise in sedation with propofol for all endoscopic procedures, including upper and lower intestinal tract endoscopic procedures. Therefore, and similarly to many other European countries, there is no requirement for an anaesthesiologist to be present during sedation in our institution. Hence, caution might be needed when introducing this sedative regimen in other institutions with less experienced nursing staff. The strengths of the present study are the large number of patients included, the diversity of bronchoscopic procedures and the original randomised non-inferiority design.

In conclusion, our data suggest that propofol is as effective and safe as combined sedation in patients undergoing flexible bronchoscopy. Therefore, propofol represents a valid alternative to combined sedation with a benzodiazepine and an opiate, particularly if timely discharge is a priority.

CLINICAL TRIALS

This trial is registered with the Current Controlled Trials database (trial number ISRCTN99754241).

SUPPORT STATEMENT

This study was supported by the Clinic of Pulmonary Medicine and Respiratory Cell Research (University Hospital Basel, Basle, Switzerland).

STATEMENT OF INTEREST

None declared.

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