UNIVERSITE DE LAUSANNE - FACULTE DE BIOLOGIE ET DE MEDECINE

Département des services de Chirurgie et d'Anesthésiologie
Service d'anesthésiologie

Comparaison de l' Ambu® aScope 2 versus fibroscope conventionnel pour l'intubation trachéale des patients avec colonne cervicale immobilisée par une minerve

THESE

préparée sous la direction du Docteur Patrick Schoettker

et présentée à la Faculté de biologie et de médecine de l'Université de Lausanne pour l'obtention du grade de

DOCTEUR EN MEDECINE

par

Vincent KRUGEL

Médecin diplômé de la Confédération Suisse
Originaire de Genève

Lausanne

2013

UNIL | Université de Lausanne
Faculté de biologie
et de médecine

Ecole Doctorale
Doctorat en médecine

Imprimatur

Vu le rapport présenté par le jury d'examen, composé de

Directeur de thèse	*Monsieur le Docteur* **Patrick Schoettker**
Co-Directeur de thèse	
Expert	*Monsieur le Docteur* **Mauro Oddo**
Directrice de l'Ecole doctorale	*Madame le Professeur* **Stephanie Clarke**

la Commission MD de l'Ecole doctorale autorise l'impression de la thèse de

Monsieur Vincent Krugel

intitulée

Comparaison de l'Ambu(R) aScope 2 versus fibroscope conventionnel pour l'intubation trachéale des patients avec colonne cervicale immobilisée par une minerve

Lausanne, le 10 septembre 2013

pour Le Doyen
de la Faculté de Biologie et de Médecine

Madame le Professeur Stephanie Clarke
Directrice de l'Ecole doctorale

Rapport de Synthèse

La prise en charge des voies aériennes est un aspect majeur de l'anesthésie dont le défaut de gestion reste la première cause de mortalité per-anesthésique.

La fibroscopie reste à l'heure actuelle une technique clé pour la gestion des situations d'intubation difficiles, mais les fibroscopes standards réutilisables sont couteux, fragiles et doivent être nettoyés et désinfectés entre chaque utilisation. L'apparition sur le marché de l'Ambu ®aScope™2, vidéoscope souple à usage unique pourrait servir d'alternative si ses capacités d'intubation dans des situations cliniques difficiles étaient démontrées.

Plusieurs études existaient démontrant l'efficacité de cet appareil sur des mannequins en situation standard ou difficile simulée, mais aucune n'avait testé son efficacité dans des situations difficiles sur patients réels, l'expérience dans se domaine se limitant à quelques case reports.

Le but de cette étude était de comparer l'Ambu ®aScope™2 au fibroscope conventionnel dans des situations d'intubation difficiles sur patients réels. Après leur accord, 100 patients prévus pour une chirurgie élective nécessitant une intubation oro-trachéale ont été répartis de façon aléatoire en deux groupes homogènes de 50. La difficulté d'intubation était induite par la mise en place d'une minerve semi-rigide après anesthésie générale, empêchant ainsi toute mobilisation cervicale et limitant grandement l'ouverture de bouche.

Les points de comparaisons étaient : Succès ou échec d'intubation, temps nécessaire pour la procédure, difficulté subjective du geste et qualité de vision des structures anatomiques.

Tous les patients ont été intubés avec succès dans les deux groupes dans des délais tout à fait satisfaisant. Cependant, le temps nécessaire à l'obtention d'un positionnement correct du tube dans la trachée était significativement plus long avec l'Ambu ®aScope™2. Par ailleurs, la qualité de vision, tout en restant suffisante pour permettre l'intubation était globalement moins bonne avec l'appareil à usage unique. Quand à la difficulté subjective du geste, elle était plus souvent classée intermédiaire ou difficile dans ce groupe, sans pour autant que la différence soit significative. Les difficultés étaient principalement dues à un manque de mobilité de la partie flexible, l'absence de canal d'aspiration des sécrétions et une lentille de moins bonne qualité, troublant la vision au contacte de la salive.

Bien que le taux de succès des intubations soit identique dans les deux groupes, il est probable que la solide expérience de l'anesthésiste en matière de fibroscopie ait permis de contourner les conditions plus difficiles du groupe de l'Ambu ®aScope™2 et ses performances techniques inférieures. Il est donc difficile de le recommander comme alternative équivalentes au fibroscope conventionnel pour les diverses situations d'intubation difficiles que l'on peut rencontre en clinique.

Anaesthesia 2013, 68, 21–26 doi:10.1111/anae.12044

Original Article

Comparison of the single-use Ambu® aScope™ 2 vs the conventional fibrescope for tracheal intubation in patients with cervical spine immobilisation by a semirigid collar*

V. Krugel,[1] I. Bathory,[2] P. Frascarolo[3] and P. Schoettker[4]

1 Staff Anaesthetist, 2 Consultant, 3 Biologist and Statistician, 4 Senior Consultant, Anaesthesiology Department, University Hospital Centre and University of Lausanne, Lausanne, Switzerland

Summary

Fibreoptic intubation remains a key technique for the management of difficult intubation. We randomly compared the second generation single-use Ambu® aScope™ 2 videoscope with a standard re-usable flexible intubating fibrescope in 50 tracheal intubations in patients with a difficult airway simulated by a semirigid collar. All patients' tracheas were intubated successfully with the aScope 2 or the re-usable fibrescope. The median (IQR [range]) time to intubate was significantly longer with the aScope 2 70 (55–97 [41–226]) s vs 50 (40–59 [27–175]) s, p = 0.0003) due to an increased time to see the carina. Quality of vision was significantly lower with the aScope 2 (excellent 24 (48%) vs 49 (98%), p = 0.0001; good 22 (44%) vs 1 (2%), p = 0.0001; poor 4 (8%) vs 0, p = 0.12) but with no difference in the subjective ease to intubate (easy score of 31 (62%) vs 38 (76%), p = 0.19; intermediate 12 (24%) vs 7 (14%), p = 0.31; difficult 7 (14%) vs 5 (5%), p = 0.76). The longer times to intubate and the poorer scores for quality of vision do not support the use of the single-use aScope 2 videoscope as an alternative to the re-usable fibrescope.

Correspondence to: P. Schoettker
Email: patrick.schoettker@chuv.ch
**Presented in part at Euroanaesthesia 2012, Paris, France.*
Accepted: 14 September 2012

In patients with difficult airways, tracheal intubation may be challenging and contribute to morbidity and mortality in anaesthesia, ranging from airway soft tissue trauma to severe hypoxaemia [1]. Despite availability of many new videoscopes and supraglottic devices [2], fibreoptic intubation remains a core skill for anaesthetists and is a key technique for the management of the difficult airway [3, 4].

Standard fibrescopes are re-usable but are expensive to purchase, in addition to costs of maintenance [5, 6]. They must be disinfected after each use, which takes time and resources and cannot be achieved perfectly because of technical property and heat sensitivity [7]. In the context of uncertainty of future implication of Creutzfeld–Jakob disease, the utilisation of single-use disposable devices are encouraged [8].

The Ambu® aScope™ (Ambu A/S, Ballerup, Denmark) is a single-use flexible videoscope [9] that has recently been introduced into clinical practice. Recent studies comparing the aScope videoscope to standard flexible re-usable fibrescopes for tracheal intubation in manikins found similar times for intubation and railroading the tubes for both devices [10]. Similarly, two studies comparing the aScope videoscope with standard flexible re-usable

fibrescopes in manikins designed to simulate difficult airways showed comparable results with regards to time of pass through the glottis and time to place the tracheal tube into the trachea [9, 11]. Despite those encouraging results, there are differences between manikins and patients, such as presence of saliva and blood or soft tissue collapse due to loss of muscle tone in anesthetised patients.

To our knowledge, there are no previous randomised clinical studies in patients comparing the aScope videoscope or the second generation aScope 2 videoscope with a standard flexible re-usable fibrescope. Experience of using the aScope videoscope in patients with difficult airways is limited to some case reports [9, 12]. Therefore, we aimed to compare the second generation single-use aScope videoscope (aScope 2) with a standard flexible re-usable fibrescope in patients with difficult airways. We choose to simulate difficulties in airway management using a properly adjusted semirigid cervical collar, which limits mouth opening and neck movement [13, 14].

Methods

After approval from the Human Research Committee of the University of Lausanne Medical School, informed written consent was obtained from 100 adult patients of ASA physical status 1 or 2 scheduled for elective surgery requiring general anaesthesia and tracheal intubation (Fig. 1). Patients with a body mass index (BMI) > 35 $kg.m^{-2}$, previous difficult intubation, cervical spine disease or injury, previous ear-nose-throat surgery or radiotherapy, gastro-oesophageal reflux, or dental instability were not studied.

Before anaesthesia, patients were randomly assigned to aScope 2 or standard flexible re-usable fibrescope groups. For the aScope 2 group, the aScope 2 was connected to the dedicated re-usable 6.5-inch liquid crystal display (LCD) situated on a table to the right of the patient and switched on. The tracheal tube was lubricated with silicon spray and inserted over the flexible part of the aScope 2. The digital camera mounted in its tip is illuminated by light emitting diodes and offers a field of view of 80°. For the standard flexible re-usable fibrescope group, we used a Pentax FB-15P (Pentax® Hoya Corporation, Tokyo, Japan). The fibrescope was connected to the Acutronic Spectral® camera and light source (Acutronic Medical Systems AG, Hirzel Switzerland) and a 15-inch LCD monitor,

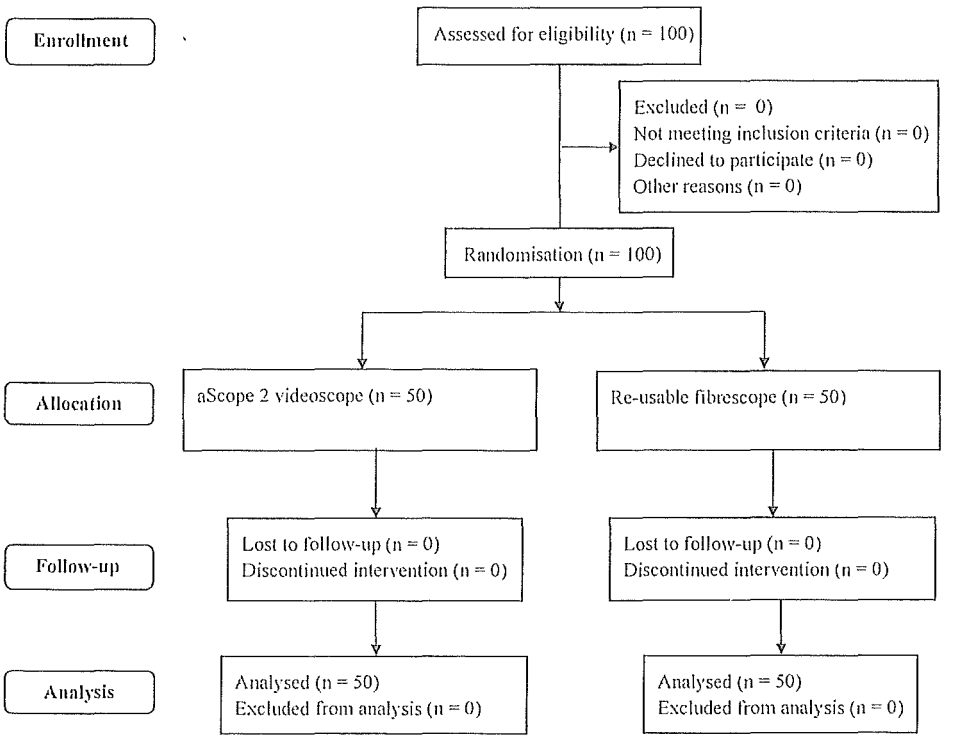

Figure 1 CONSORT flow diagram of the study.

which was situated on the right side of the patient. A suction source was connected to the instrument channel. The tracheal tube was lubricated and inserted over the flexible part of the fibrescope. The monitor and the camera were then switched on with white balance and focus adjusted.

All tracheal intubations were performed using a standard 6.5-mm tube for female patients and a 7.5-mm tube for male patients (Mallinckrodt® Hi-Contour Oral Tracheal Tube Cuffed; Covidien llc, 15 Hampshire Street, Mansfield, MA, USA).

Pre-operative evaluation and anaesthesia were provided by the anaesthetist in charge of the patient, in accordance with the standard practice of our department. After pre-oxygenation by facemask for 3–5 min to obtain an end-expiratory oxygen concentration >90%, anaesthesia was induced by administering propofol (2 $mg.kg^{-1}$) and analgesia was provided by fentanyl (3 $\mu g.kg^{-1}$). Neuromuscular blockade was achieved with rocuronium (0.6 $mg.kg^{-1}$).

During facemask ventilation, neck circumference (at the level of the thyroid cartilage), thyromental distance and maximal mouth opening were measured. The neck was then immobilised with an appropriate sized semi-rigid Philadelphia Patriot® cervical collar (Philadelphia Cervical Collar Co., Thorofare, NJ, USA) [15] and maximal mouth opening with cervical collar was again measured.

An Ovassapian split oral airway was then inserted into the mouth to facilitate introduction of the aScope 2 or fibrescope from teeth to epiglottis [16].

The timer was started (T0) when touching the aScope 2 or fibrescope, which was then inserted through the Ovassapian oral airway into the trachea. Once the carina was identified, the time was recorded (T1). The Ovassapian split oral airway was then removed and the tube was railroaded over the aScope 2 or fibrescope through glottis and trachea. The aScope 2 or fibrescope was withdrawn, the tube connected to the ventilator and the timer stopped when correct tracheal positioning confirmed by observation of the end-expiratory CO_2 curve on capnography (T2). Oxygen saturation (S_pO_2) was noted after pre-oxygenation and at the end of the procedure.

Tracheal intubation was considered failed if it could not be accomplished within 4 min or in the event of desaturation (S_pO_2 < 95%) before identification of the carina. If for any reason (cleaning the optics or insufficient suctioning) the intubation process had to be interrupted before 4 min, the timer was reset and a new attempt was performed. In case of excessive subjective difficulty to see the glottis, a jaw-thrust manoeuvre was performed to improve patency of the upper airways [17].

All 100 patients' tracheas were intubated by the same experienced anaesthetist who had previously performed > 20 aScope intubations and >60 standard flexible fibreoptic intubations. Quality of vision was defined as 'excellent' if all airway structures could be easily recognised and the picture quality was sharp on the entire screen; 'good' if the airway structures could be recognised and at least half of the screen was clear of fogging or secretions; and 'poor' if fogging or secretions affected more than half of the screen. Ease of intubation was scored as 'easy' if insertion and manoeuvrability were achieved without any problems, 'intermediate' in cases of difficulty or resistance in passing the 'scope and 'difficult' in cases of limitation of device insertion or manoeuvrability.

The primary endpoint was the total intubation time (T2-T0). Secondary endpoints included time to identify carina (T1-T0), tube railroading time (T2-T1), jaw-thrust manoeuvres required, intubation success rate, S_pO_2 before and at the end of intubation procedure, quality of vision on the monitors and subjective assessment of ease of intubation.

Sample size calculation (a 20-s expected difference of intubation times with an expected SD of 50 s, a desired power of 0.8 and a p of 0.05) yielded a required sample size of n = 50 per group to detect statistically significant group differences.

Statistical tests used were median or chi-squared where appropriate. Data were analysed using the JMP 10 statistical package (SAS Institute Inc., Cary, NC, USA).

Results

Both groups were similar in terms of sex, ASA status, weight and height, and no statistically significant difference was noted in factors predictive of difficult intubation (Table 1).

All the patients' tracheas were intubated successfully in both groups with the dedicated scope. The median

Table 1 Characteristics of patients randomly assigned to the aScope™ 2 videoscope or flexible fibrescope. Data are shown as number or median (IQR [range]).

	aScope 2	Fibrescope
Male/female	27/23	25/25
ASA physical status	2 (1–2 [1–2])	2 (1–2 [1–2])
Weight; kg	74 (65–85 [45–98])	70 (62–81 [50–110])
Height; cm	170 (162–177 [150–187])	170 (163–180 [152–191])
BMI; $kg.m^{-2}$	26 (23–29 [20–35])	25 (21–28 [18–33])
Mallampati score	1 (1–2 [1–3])	1 (1–2 [1–3])
Thyromental distance; cm	8 (7–9 [5–10])	8 (7–8 [6–9])
Neck circumference; cm	40 (35–42 [30–48])	38 (35–41 [30–52])
Mouth opening without cervical collar; cm	5 (4–5 [3–7])	5 (4–5 [3–6])
Mouth opening with cervical collar; cm	2 (2–2 [1–3])	2 (2–2 [1–3])

time to intubate was significantly longer in the aScope 2 group (Table 2). Median time for carina identification was significantly longer in the aScope 2 group compared with the fibrescope group, whereas the time required for railroading the tube was identical (34 s vs 32 s, p = 0.07). No differences were noted in time to railroad between female (6.5-mm tube) and male patients (7.5-mm tube).

A jaw-thrust manoeuvre was needed significantly more often in the aScope 2 group compared with the fibrescope group (16 (32%) vs 5 (10%) patients; p = 0.01). Four patients needed two attempts in the aScope 2 group, due to secretions that necessitated removal of the videoscope and cleaning of the lens, compared with eight with the fibrescope (p = 0.22), due to secretions (one patient), malpositioning of the Ovassapian split oral airway (two patients) and accidental withdrawal of fibrescope during manipulations (five patients). No episodes of desaturation were reported.

Subjectively, quality of vision was considered excellent in fewer than half of the aScope 2 intubations but in nearly all intubations with the fibrescope (24 (48%) vs 49 (98%), p = 0.0001). For the remaining intubations, quality of vision was described as good in 22 (44%) vs 1 (2%), p = 0.0001 and poor in 4 (8%) vs 0, due to fogging and inability of cleaning the lens after contact with saliva or secretions.

Ease of intubation was described as 'easy' for fewer procedures in the aScope 2 vs conventional fibrescope groups (31 (62%) vs 38 (76%)), but this was not statistically significant (p = 0.19), with 'intermediate' (12 (24%) vs 7 (14%) p = 0.31) and 'difficult' (7 (14%) vs 5 (5%) p = 0.76). These subjective measures encompassed assessment of device handling, device positioning and tube railroading. The procedures described as 'difficult' were due to problems due to secretions and lack of mobility of the tip, particularly downward in the aScope 2 group, whereas difficulties were principally attributed to the weight of the camera on the fibrescope and secretions in the fibrescope group.

Table 2 Times to intubate the trachea with the aScope 2 videoscope or the flexible fibrescope. Data are shown as median (IQR [range]).

	aScope 2	Fibrescope	p
T1; s	28 (22–46 [16–206])	15 (12–22 [7–110])	0.0001
T2; s	70 (55–97 [41–226])	50 (40–59 [27–175])	0.0003

T1: Time from starting clock to identifying the carina.
T2: Time from starting clock to observing end-tidal CO_2 on capnography.

No changes in times to see the carina or tracheal intubation were noticed over the course of the study, excluding a 'learning' component.

Discussion

The main results of this study offer little support for the use of aScope 2 as an alternative to the conventional device. The median time to intubate was longer with the aScope 2, more jaw thrust manoeuvres were needed, and there were fewer 'excellent' ratings of quality of vision. Yet, overall success rates for intubation were similar, perhaps suggesting that anaesthetists use their skills to overcome intrinsic technical difficulties of the device.

The longer intubation times with the aScope 2 were essentially due to an increased time to identify the

carina. The tip of the single-use device is characterised by a lesser range of movement, with a limited angulation (120° up and down, whereas the standard fibrescopes presents a tip mobility of 180° up and 130° down). This might make it difficult to pass under the tongue or a falling epiglottis. Extreme downward bending is difficult to achieve in specific situations, and although the tip angulation is described as equal in the up or down movement, its mobility is better obtained upwards. Subjectively, the aScope 2 tip is perceived as softer, therefore rendering its progression occasionally more difficult. However, we, could not show a 'learning effect' and the single intubator commented on these issues throughout the study. Similar findings were described in a manikin and clinical study by Piepho et al. [9] in which participants described the aScope as less rigid than the standard intubation fibrescope. However, unlike in our study, they found no differences in intubation time between the two devices for the five fibreoptic intubations that were performed on patients.

Another functional difference is the lack of suctioning channel on the aScope 2. This was subjectively considered as a deficiency in some tracheal intubations in our study with this device and a reason why a second attempt was necessary in four out of 50 cases. It is therefore of particular importance to avoid contact with mucosa or secretions when using the aScope 2, as this results in considerable loss of quality of vision. Vijayakumar et al. [11] used the tip surface count to compare the manoeuvrability between the aScope videoscope and a conventional fibrescope and could not show a difference. The absence of a suctioning channel on the aScope 2 could lead to problems in specific patients.

Yet, compared with the fibrescope, the aScope 2 has several theoretical advantages. First, it is light and easy to manipulate for each step by one operator only. We found in some cases that the weight of the camera attached to the standard fibrescope often required an extra hand to hold the device during railroading, leading to accidental displacement of the tracheal tube over the fibrescope (five times) necessitating a second attempt to intubate, as described by Pandit et al. [18]. Second, the time required for the intubation device to be ready to work is much shorter with the aScope 2 videoscope. In our institution, well-trained anaesthetists required 15 s to remove the aScope 2 from the package, turn on the screen, plug the cable and switch on the device, which is immediately ready for use without the need of adjust the focus and the brightness. In contrast, a minimum of 40 s is needed for the similarly trained anaesthetists to make the conventional fibrescope ready for use, and although experienced operators can manipulate a conventional fibrescope very quickly, technical issues can be limiting. Similar problems were highlighted by Pandit et al. [18]. The light weight of the aScope 2 makes it easy to transport from one operating room to another, unlike a standard fibrescope attached to its camera and screen trolley.

Conventional fibrescopes are re-usable but initially expensive devices. Costs not only include the price of fibrescope, external camera and video monitor, but those of cleaning, maintenance and repairs. As reported in a recent study [5], the cost of most flexible videoscopes like the aScope 2 does not depend on use as the unit price is fixed. In contrast, the cost per intubation declines as the frequency of use of the re-usable fibrescopes rises, as the cleaning costs are trivial compared with outlay costs. Therefore, every institution should properly assess its own need for the type of fibrescopes or videoscopes depending on indications for fibrescopy, hospital setting, staff and equipment issues. The evidence that conventional fibrescopes promote infectious diseases is still under scrutiny and in cases of expected difficult airways, a proper balance between risks and benefits must be established [5].

The current study has some limitations. First, all of the intubations were performed by the same anaesthetist experienced in fibrescopy. Depending on the experience of the provider, especially in cases of suboptimal vision or abundant secretions, differences in intubation success rates and times might become apparent. Second, difficult airway management was simulated in our study using a semirigid collar producing limited mouth opening and neck movement. In cases of airway malignancy leading to disturbed anatomy or excessive secretions, the performance of both devices may be significantly different.

In conclusion, we find little evidence to support the notion that the new single-use flexible aScope 2 videoscope represents an alternative to the conventional fibrescope. Shortcomings have been identified due to the

quality of the apparatus, the lack of a suction lumen and a low performance lens. A case-by-case analysis of the setting and the reasons of fibrescopy should be carried out in each institution to decide which alternative – i.e. re-usable or single-use – is the best solution.

Acknowledgements

We thank the Fondation Latine des Voies Aériennes (FLAVA http://www.flava.ch) for purchasing the 50 aScopes 2® used in this study.

Competing interests

No other external funding or competing interests declared.

References

1. Peterson GN, Domino KB, Caplan RA, Posner KL, Lee LA, Cheney FW. Management of the difficult airway: a closed claims analysis. *Anesthesiology* 2005; **103**: 33–9.
2. Frerk CM, Lee G. Laryngoscopy: time to change our view. *Anaesthesia* 2009; **64**: 351–4.
3. American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. *Anesthesiology* 2003; **98**: 1269–77.
4. Henderson JJ, Popat MT, Latto IP, Pearce AC. Difficult Airway Society guidelines for management of the unanticipated difficult intubation. *Anaesthesia* 2004; **59**: 675–94.
5. Tvede MF, Kristensen MS, Nyhus-Andreasen M. A cost analysis of re-usable and disposable flexible optical scopes for intubation. *Acta Anaesthesiologica Scandinavica* 2012; **56**: 577–84.
6. Gupta D, Wang H. Cost-effectiveness analysis of flexible optical scopes for tracheal intubation: a descriptive comparative study of re-usable and single-use scopes. *Journal of Clinical Anesthesia* 2011; **23**: 632–5.
7. Medical Devices Agency Decontamination of Endoscopes – DB 2002(05). *Medical Devices Agency*. http://www.mhra.gov.uk/publications/Safetyguidance/DeviceBulletins/CON007329 (accessed 09/09/2012).
8. Association of Anaesthetists of Great Britain and Ireland Infection control in anaesthesia. *Anaesthesia* 2008; **63**: 1027–36.
9. Piepho T, Werner C, Noppens RR. Evaluation of the novel, single-use, flexible aScope for tracheal intubation in the simulated difficult airway and first clinical experiences. *Anaesthesia* 2010; **65**: 820–5.
10. Scutt S, Clark N, Cook TM, et al. Evaluation of a single-use intubating videoscope (Ambu aScope) in three airway training manikins for oral intubation, nasal intubation and intubation via three supraglottic airway devices. *Anaesthesia* 2011; **66**: 293–9.
11. Vijayakumar M, Clarke A, Wilkes AR, Goodwin N, Hodzovic I. Comparison of the manoeuvrability and ease of use of the Ambu aScope and Olympus re-usable fibrescope in a manikin. *Anaesthesia* 2011; **66**: 689–93.
12. Pujol E, Lopez AM, Valero R. Use of the Ambu((R)) aScope in 10 patients with predicted difficult intubation. *Anaesthesia* 2010; **65**: 1037–40.
13. Goutcher CM, Lochhead V. Reduction in mouth opening with semi-rigid cervical collars. *British Journal of Anaesthesia* 2005; **95**: 344–8.
14. Bathory I, Frascarolo P, Kern C, Schoettker P. Evaluation of the GlideScope for tracheal intubation in patients with cervical spine immobilisation by a semi-rigid collar. *Anaesthesia* 2009; **64**: 1337–41.
15. Tescher AN, Rindflesch AB, Youdas JW, et al. Range-of-motion restriction and craniofacial tissue-interface pressure from four cervical collars. *Journal of Trauma* 2007; **63**: 1120–6.
16. Truong A, Truong DT. Use of a modified Ovassapian airway to increase mouth opening for fiberoptic orotracheal intubation in a patient with severe trismus. *Anesthesia and Analgesia* 2011; **113**: 958–9.
17. Albrecht E, Schoettker P. Images in clinical medicine. The jaw-thrust maneuver. *New England Journal of Medicine* 2010; **363**: e32.
18. Pandit JJ, Dravid RM, Iyer R, Popat MT. Orotracheal fibreoptic intubation for rapid sequence induction of anaesthesia. *Anaesthesia* 2002; **57**: 123–7.