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SHORT COMMUNICATIONS

Safety of patient-maintained propofol sedation using a target-controlled system in healthy volunteers†

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We investigated the safety of a patient-maintained system that allows individuals to operate a target-controlled infusion of propofol to achieve sedation. Ten healthy volunteers were recruited and instructed to try to anaesthetize themselves with the system. A target-controlled infusion of propofol was set to deliver a target propofol concentration of 1 μg ml^{-1}, and the subjects allowed to increase the target in increments of 0.2 μg ml^{-1} by pressing a control button twice in 1 s. There was a lockout time of 2 min and a maximum permitted target concentration of 3 μg ml^{-1}. Heart rate and pulse oximetry oxygen saturation (Sp_{O_2}) were monitored continuously, and non-invasive arterial pressure, ventilatory frequencies and sedation scores were measured every 5 min. Sedation was continued until the subject stopped pressing the button. A keyword was then read for the individual to remember and sedation discontinued. There were no instances of significant decrease of Sp_{O_2} or loss of airway control. Maximum target blood concentration of propofol recorded ranged from 1.4 to 3 μg ml^{-1}. Two subjects became oversedated, one of whom was unrousable with loss of eyelash reflex. No subject could recall the keyword, although one recognized it from a list of 10 words. We conclude that the patient-maintained sedation system described could not be guaranteed to produce only conscious sedation in all patients, and that close clinical supervision by an anaesthetist would still be required for safe operation.

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Patient-controlled sedation systems, which administer bolus doses of the agent, have been studied by other investigators and found to be both an effective[1] and popular[2] technique for patients undergoing surgery under regional anaesthesia. A patient-maintained sedation system, which delivers a target-controlled infusion of propofol, has also been used successfully to provide sedation for patients undergoing orthopaedic surgery,[3] and more recently as an anxiolytic premedication for patients undergoing day surgery.[4] With any system in which the patient has control of sedative administration, a major concern is safety, as regards the depth of sedation that can be achieved and the maintenance of cardiorespiratory function. The goal of any patient-controlled sedation system should be delivery of conscious sedation while operating safely to prevent oversedation. Ultimately this safety depends on the appropriateness of the staged increase in dose of the sedative drug, the effectiveness of the lockout interval in allowing equilibration of the drug with the effect site, and the ability of the subject to coordinate a successful push of the control button. These three elements should function together in a feedback loop to prevent oversedation in all situations, including that in which individuals might be determined to administer as much sedative as possible through repetitive operation of the control button. We aimed to test the feedback loop of our system, in such a situation, in healthy volunteers who were asked to operate the system repetitively in an attempt to anaesthetize themselves.

†This research was presented in part at the Annual Meeting of the American Society of Anesthesiologists, Dallas, 1999.

Methods and results

Local Ethics Committee approval for the study and written informed consent were obtained from 10 healthy adult volunteers, aged 18–40 yr. The exclusion criteria were a history of intercurrent disease, cardiorespiratory, renal or hepatic dysfunction, psychiatric disorder or mental retardation, use of any medication with sedative effects or a history of anaesthetic problems. The experimental target-controlled infusion (TCI) system used for sedation consisted of a Graseby 3400 infusion pump, the rate of which was controlled by a backbar microprocessor programmed with pharmacokinetic data describing the distribution and elimination of propofol.[5] By entering the subject's age and weight, and the desired initial blood concentration of propofol, the system calculates the initial bolus and variable infusion rates to achieve and maintain this concentration as given by the pharmacokinetic model, and gives a calculated figure for 'effect site concentration'.[6] Connection of a control button to the backbar enables the subject to increase the target blood concentration (C_T) of propofol in increments of 0.2 μg ml^{-1} by double pressing the button within 1 s. There is then a lockout period of 2 min during which no further increase is possible with a maximum attainable target concentration of 3 μg ml^{-1}. If no successful presses are detected for a period of 6 min, there is a stepped reduction in the target concentration to a minimum of 0.2 μg ml^{-1}.[3,4]

Before starting the sedation, the subjects were instructed in the use of the control button and allowed to get the feel of its operation. They were instructed to press the button as often as they could in an attempt to anaesthetize themselves. Measurement of non-invasive arterial pressure (NIBP), heart rate (HR), ventilatory frequency and pulse oximetry oxygen saturation (Sp_{O_2}) were recorded, and a 21G intravenous cannula sited. A target-controlled intravenous infusion of propofol (1% with lignocaine 20 mg per 50 ml) was started at an initial target concentration of 1 μg ml^{-1}, and time allowed for the calculated effect site concentration, as determined and displayed by the system,[6] to reach within 0.1 μg ml^{-1} of the set blood target level. The control button was then activated and the subject reminded to double press it as often as possible. One further verbal encouragement to push the button was given during the study period if they failed to push it for more than 3 min.

Heart rate and Sp_{O_2} were monitored continuously, NIBP, ventilatory frequency and sedation score, using a modified Steward sedation score,[3] were measured every 5 min following the start of sedation. Sedation scores were assessed by one of the two authors, who were familiar with the assessment and scoring of sedation levels. Oversedation was defined as loss of response to verbal command. An Sp_{O_2} <94% or ventilatory frequency <8 were considered clinically significant and were to be treated with supplementary oxygen. A decrease in baseline NIBP or HR >30% or HR <50 min^{-1} were to be treated as considered appropriate by the investigator.

Table 1 Subject characteristics, sedation scores, maximum target concentrations (C_T) and dose of propofol and total sedation time. All values given as median (range) or number

Age	31 (23–40)
Weight (kg)	77.5 (57–86)
Sex (m : f)	9 : 1
Sedation scores when demands ceased:	**Number of subjects**
Consciousness	
4 Fully awake	0
3 Lightly asleep, spontaneous eye opening	3
2 Eyes open on command	5
1 Responding to ear pinching	1
0 Unresponsive	1
Airway	
3 Opening mouth, cough on command	3
2 Clear unsupported airway	7
1 Airway obstructed on neck flexion only	0
0 Airway obstructed without support	0
Activity	
2 Raise arm on command	5
1 No purposeful movement	4
0 No movement	1
Maximum C_T propofol (μg ml^{-1})	2.0 (1.4–3.0)
Time (min)	29.5 (9–46)
Dose of propofol (μg kg^{-1} min^{-1})	88.3 (73.5–142.3)

Any sign of anaesthesia, such as loss of verbal contact or loss of eyelash reflex, was recorded. Sedation was discontinued if the subject became unresponsive or failed to double press the control button on three attempts or for a period of more than 3 min, if there was loss of airway control, pulse oximetry oxygen desaturation below 94% on room air, or the target concentration reached the maximum level of 3 μg ml^{-1}. This was the primary end point at which the deepest level of sedation achieved, the greatest predicted blood and corresponding 'effect site concentration' of propofol reached were recorded. At this time a keyword was read for the subject to remember. One hour after discontinuing the sedation, subjects were asked to repeat the keyword. If unable to do so a list of 10 words including the keyword was read out and again the subject was asked to identify it.

Ten healthy volunteers were recruited to the study. Subject characteristics are shown in Table 1. Maximum Steward sedation scores ranged from 2 to 8 with a median of 5, scores for consciousness, airway and activity at the maximum C_T propofol reached are shown in Table 1. Maximum C_T propofol reached ranged from 1.4 to 3.0 μg ml^{-1} with a median of 2 μg ml^{-1}. The total dose of propofol administered ranged from 105 to 351 mg.

For seven of the subjects, the difference between maximum C_T propofol reached and the C_T at which the subject first failed to double press the control button were within 0.2 μg ml^{-1} (equivalent to one successful press). Three of the subjects, who could not coordinate a double

press, were still able to single press the control button at the maximum sedation. Two subjects did not respond to speech, and one was unrousable to painful stimulus, at 1.4 μg ml^{-1} with loss of eyelash reflex. There were no instances of significant decrease in Sp_{O_2} or loss of airway control.

No subject had automatic recall of the keyword, although one, whose lowest score for consciousness score was 3 at the maximum C_T propofol of 3 μg ml^{-1}, recognized it when it was read from the list.

Comment

Our system functioned to prevent oversedation in 80% of the subjects studied, all of whom were actively trying to anaesthetize themselves. For these individuals the feedback loop provided by the patient control button functioned well. The need to double press the button appeared to be an important safety factor for three individuals who could not coordinate a double press at maximum sedation level. However, two subjects became oversedated, with one displaying signs of anaesthesia. It is possible that our increments of C_T propofol 0.2 μg ml^{-1} and 2-min lockout time failed to provide an adequate feedback loop. Reducing the staged increments in target concentration, and so delivery dose, with each successful press and increasing lockout time could allow more complete equilibration of blood and effect site concentrations of propofol and, therefore, could reduce the incidence of oversedation.

Thorpe and colleagues[7] studied 100 patients who were asked to anaesthetize themselves with a system delivering boluses of propofol with no lockout period. They reported an 11% incidence of oversedation with 2% reaching unresponsiveness. The total doses of propofol that their patients self-administered varied over a fourfold range from 66 mg to 248 mg. The twofold range of maximum target concentrations reached by our volunteers is likely to be a combination of the error inherent in estimates of predicted blood propofol levels (pharmacokinetic variability) and the predictable variability in pharmacodynamic response to propofol, reinforcing the need for careful titration of sedation according to individual needs. This variability makes it difficult to design a foolproof system to prevent oversedation.

For our subjects the motivation to press the control button relied entirely on the initial instruction given and one reinforcement on their first failure. This repeat instruction was given in an attempt to mirror the clinical situation where individuals will respond to heightened stimulation by pressing the control button. However, for ethical reasons, it is clearly difficult to recreate such surgical conditions and we acknowledge that our subjects were not exposed to any real clinical stimulation.

It is interesting that none of the volunteers had spontaneous recall of keywords, indicating that all had reached an amnesic level of sedation. Implicit memory could account for the recognition of the keyword by one volunteer, although this could equally be a chance finding.

In conclusion, the fact that two individuals became oversedated, with one showing signs of anaesthesia, indicates that, in its existing form, the patient-maintained sedation system described could be not guaranteed to produce conscious sedation in 100% of subjects instructed to attempt to anaesthetize themselves. How accurately this would reflect real clinical use may be debated, but we must conclude that close clinical supervision by an anaesthetist would be required to operate this system safely. However, the blood concentration of propofol decreases rapidly when the drug infusion is discontinued which would allow rapid recovery to a state of conscious sedation for those individuals who were oversedated. Further investigations looking at the effects of altering incremental doses and lockout times on improvement of the feedback loop are warranted.

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Rapacuronium recovery characteristics and infusion requirements during inhalation *versus* propofol-based anaesthesia

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We examined the effect of four maintenance anaesthetics on the neuromuscular blocking activity and spontaneous recovery characteristics after a short-term infusion of rapacuronium. Eighty ASA I–III adult patients undergoing elective surgery were studied at four centres. Anaesthesia was induced with propofol 1.5–2.5 mg kg^{-1} and fentanyl 1–2 μg kg^{-1}, followed by a bolus of rapacuronium 1.5 mg kg^{-1}. The patients were randomized to receive either desflurane (2–4% end-tidal, ET), sevoflurane (0.75–1.5% ET), isoflurane (0.4–0.8% ET), or a propofol infusion (75–150 μg kg^{-1} min^{-1}) for maintenance of anaesthesia in combination with nitrous oxide (60–70%) in oxygen. When the first twitch (T_1) of a train-of-four stimulus (using the TOF Guard® accelerometer) returned to 5%, an infusion of rapacuronium was started at 3 mg kg^{-1} h^{-1} and adjusted to maintain T_1/T_0 at 10%. The duration of infusion lasted between 45 and 60 min, and the average infusion rates of rapacuronium were similar in all groups, ranging from 1.6 to 2.5 mg kg^{-1} h^{-1}. There were no significant differences among the groups in the times for T_1/T_0 to return to 25%, 75% or 90%, or for T_4/T_1 to return to 70% and 80% upon discontinuation of the infusion. When potent inhalation anaesthetics are used in clinically relevant concentrations for maintenance of anaesthesia, the neuromuscular recovery profile of rapacuronium administered as a variable-rate infusion for up to 1 h is similar to that found with a propofol-based anaesthetic technique.

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Rapacuronium (ORG 9487) is a new aminosteroidal non-depolarizing neuromuscular blocking drug which has a rapid onset and short duration of action following an i.v. bolus dose.[1] In a preliminary study, van den Broek and colleagues reported that when a short-term (1 h) infusion of rapacuronium was administered during isoflurane anaesthesia, its time course of recovery was altered from that of a short- to an intermediate-acting neuromuscular blocking drug.[2] However, there are a lack of data pertaining to the relative potentiating effect of different maintenance anaesthetics on rapacuronium-induced blockade.

Thus, we evaluated the neuromuscular blocking effects and spontaneous recovery profile when a continuous infusion of rapacuronium was administered during general anaesthesia maintained with equipotent concentrations of either desflurane, sevoflurane or isoflurane *versus* propofol in combination with nitrous oxide (N_2O).

Methods and results

After obtaining institutional review board approval and written informed consent, 80 ASA I–III patients aged between 18 and 70 yr, undergoing elective orthopaedic and general surgery procedures with an anticipated duration of at least 2 h, were enrolled at four United States medical centres. Exclusion criteria included clinically significant hepatic, renal or neuromuscular disease, pregnancy, anticipated difficult intubation, drug therapy known to modify neuromuscular blockade (e.g. anticonvulsants, aminoglycoside/polypeptide antibiotics) and those whose body weight was 30% above or below their ideal body weight. The

investigation was designed as an open-label, parallel-group comparative, multicentre study in which patients were randomized in groups of 20 at each centre to receive either desflurane (n=5), sevoflurane (n=5), isoflurane (n=5) or propofol (n=5) in combination with nitrous oxide for maintenance of general anaesthesia.

Midazolam 1–3 mg i.v. was administered for premedication 10–15 min prior to induction of anaesthesia. Non-invasive blood pressure, electrocardiogram (ECG) and haemoglobin oxygen saturation ($S_{p_{O_2}}$) were monitored. Anaesthesia was induced with propofol 1.5–2.5 mg kg^{-1} and fentanyl 1–2 μg kg^{-1} i.v.. Mask ventilation with 100% oxygen was instituted while the baseline measurements of neuromuscular function were obtained using a TOF Guard® accelerometer (Organon Teknika NV, Belgium). The TOF Guard® electrodes, temperature thermistor-sensor and accelerometric transducer were positioned on the patient's arm prior to induction of anaesthesia, and the arm was carefully secured to the operating table armboard during the study period in order to obviate inadvertent movements which may produce artifactual readings. After obtaining a stable T_1 recording (baseline value), rapacuronium 1.5 mg kg^{-1} was injected over 5 s into a rapidly flowing peripheral i.v. line in the opposite arm. The patient was intubated within 90 s and mechanical ventilation was initiated to maintain the end-tidal (ET) carbon dioxide (CO_2) at 4.5–5.0 kPa.

Maintenance of anaesthesia consisted of either desflurane (2–4% ET), sevoflurane (0.75–1.5% ET), isoflurane (0.4–0.8% ET) or propofol infusion (75–150 μg kg^{-1} min^{-1}) in combination with 60–70% nitrous oxide in oxygen according to a computer-generated randomization scheme. The patients received fentanyl 1 μg kg^{-1} and/or labetalol 5–10 mg as needed to maintain haemodynamic stability. Central (oesophageal) and peripheral (axillary) temperatures were monitored and maintained above 36.5 °C and 32.5 °C, respectively, using a forced-air warming blanket. All patients received crystalloids (Plasmalyte®), with colloids or blood only administered if indicated.

When T_1/T_0 returned to 5%, a continuous infusion of rapacuronium was started at 3 mg kg^{-1} h^{-1} and adjusted to maintain T_1/T_0 at 10% for 45–60 min. After discontinuation of the rapacuronium infusion, the patients were allowed to recover spontaneously until the times for return of T_1/T_0 to 25%, 75% and 90%, as well as the times for return of T_4/T_1 to 70% and 80% were recorded, if clinically feasible. If the T_4/T_1 ratio was <70% at the end of surgery, a combination of neostigmine 50–70 μg kg^{-1} and glycopyrrolate 8–10 μg kg^{-1} was administered to reverse residual neuromuscular blockade.

Based on an earlier study involving a rocuronium infusion,[3] an *a priori* power analysis suggested that a sample size of 20 subjects per treatment group would provide at least 80% power for detecting a difference of one standard deviation in infusion rates between any two treatment groups at the P=0.05 significance level. The SAS (version 6.09) computer software package used for data analysis was run on a VMS operating system. Frequency and univariate procedures were used for summary statistics, and two-way analyses-of-variance using general linear models procedures were used for analysis of infusion rates and recovery variables. Data are presented as mean (SD), medians or numbers (Table 1), with P-values <0.05 considered statistically significant.

Although 80 patients were enrolled, five were excluded from the analysis because of protocol violations at the onset of the study, while subsequent violations precluded analysis of one patient who received the rapacuronium infusion for only 26 min and four patients who received additional anaesthetic agents before the end of the rapacuronium infusion. There were no significant differences in the patient characteristics (Table 1), rapacuronium infusion times (group means from 53 to 55 min), total rapacuronium dosages (group means from 3.4 to 3.9 mg kg^{-1}) and average rapacuronium maintenance infusion rates to maintain ~90% block (group means from 1.6 to 2.5 mg kg^{-1} h^{-1}) among the four anaesthetic groups. The maintenance dosages (MAC h^{-1}) of the potent inhalation agents were similar in the desflurane, sevoflurane and isoflurane groups. There were also no statistical differences in the times for T_1/T_0 recovery to 25%, 75% and 90%, or for T_4/T_1 to recover to 0.7 and 0.8 (Table 1).

Comment

In this study, the recovery times after discontinuing the infusion of rapacuronium were significantly longer than following a single intubating dose of rapacuronium.[1] These findings confirm a previous report which suggested that rapacuronium was altered from a short-acting to an intermediate-acting neuromuscular blocking drug when administered as an infusion.[2] The apparent pharmacodynamic change may be explained by the reduced contribution of distribution to plasma clearance, as well as the accumulation of the 3-desacetyl metabolite of rapacuronium (ORG 9488), which has a longer half-life and appears to be more potent than the parent compound.[4] Van den Broek and colleagues[2] demonstrated that a TOF ratio of 0.7 measured by mechanomyography (MMG) was attained 38 min after a 1 h infusion of rapacuronium, which was significantly shorter than the times reported in our study (71–92 min). This difference may be related in part to the less profound depth of neuromuscular blockade established in the earlier study (83% *versus* 92%, respectively), and the variations in recovery profiles as a result of using acceleromyography *versus* MMG monitoring.[5]

Desflurane, sevoflurane and isoflurane all potentiate the neuromuscular blockade produced by non-depolarizing neuromuscular blocking drugs,[6 7] whereas most studies have failed to demonstrate potentiation with propofol.[8 9] We compared these potent inhalation anaesthetics to a propofol infusion for maintenance of anaesthesia and no statistically

Table 1 Physical characteristics, neuromuscular recovery and infusion rate data for the four study groups.* Data are expressed as means (SD), medians or numbers (*n*), age, range. ASA, American Society of Anesthesiologists; NA, non-applicable; MAC h^{-1}, sum of end-tidal concentration divided by the minimum alveolar concentration (MAC) value (adjusted for concomitant use of nitrous oxide and age) multiplied by the duration (h) at that concentration. Rapacuronium infusion rate = mean infusion rate of rapacuronium at 40 min after starting the maintenance infusion. Recovery index=time interval between recovery of T_1/T_0 to 25% and 75%. *There were no significant differences among the four study groups

	Desflurane	Sevoflurane	Isoflurane	Propofol
Age (yr)	51 (00–00)	50 (00–00)	47 (00–00)	53 (00–00)
Height (cm)	168 (11)	167 (12)	166 (10)	171 (9)
Weight (kg)	70 (15)	80 (20)	72 (16)	78 (20)
Sex (M/F)	16/4	15/5	14/6	16/4
ASA (I/II/III)	7/11/2	5/12/3	9/11/0	3/16/1
Potent inhaled anaesthetic (MAC h^{-1})	4.1 (2.5)	3.8 (2.1)	4.4 (2.2)	NA
Propofol infusion rate (μg kg^{-1} min^{-1})	NA	NA	NA	119 (30)
Rapacuronium infusion rate (mg kg^{-1} h^{-1})	2.3 (0.7) (2.4) (*n*=20)	1.6 (0.8) (1.7) (*n*=20)	2.5 (1.6) (2.4) (*n*=19)	2.2 (1.3) (2.3) (*n*=20)
Time (min) to				
T_1/T_0 = 25%	15.3 (12.5) (10.3) (*n*=19)	19.9 (22.8) (12.0) (*n*=20)	13.3 (7.3) (13.2) (*n*=17)	10.5 (7.7) (7.8) (*n*=20)
T_1/T_0 = 75%	35.6 (17.1) (28.2) (*n*=15)	55.7 (41.8) (44.4) (*n*=14)	44.1 (27.9) (36.1) (*n*=14)	32.6 (16.5) (25.8) (*n*=17)
T_1/T_0 = 90%	39.5 (22.9) (30.8) (*n*=11)	73.3 (49.5) (79.2) (*n*=13)	60.1 (34.6) (56.6) (*n*=10)	37.5 (15.9) (32.3) (*n*=14)
T_4/T_1 = 0.7	73.0 (24.8) (79.9) (*n*=10)	106.7 (34.0) (115.4) (*n*=6)	85.0 (42.5) (82.8) (*n*=10)	70.6 (23.4) (68.5) (*n*=13)
T_4/T_1 = 0.8	83.4 (30.0) (84.0) (*n*=8)	139.5 (36.8) (130.5) (*n*=5)	85.4 (42.5) (70.9) (*n*=4)	82.1 (23.6) (85.6) (*n*=11)
Recovery index (min)	25.0 (14.3) (24.1) (*n*=15)	36.8 (28.6) (34.4) (*n*=14)	34.6 (24.0) (26.3) (*n*=14)	24.1 (15.0) (19.2) (*n*=17)

significant differences were found with respect to the recovery characteristics following an equi-effective rapacuronium infusion, although the mean values in the sevoflurane group did tend to be longer. These results are analogous to those of Wulf and colleagues[9] who demonstrated that spontaneous recovery of neuromuscular function following rocuronium was similar during propofol or volatile-based anaesthesia using a TOF Guard® monitor.

The failure to find any significant differences among the four anaesthetic techniques may be attributed to: (i) the limited sample sizes especially for the later recovery variables (due to the difficulty in accurately predicting the need for further muscle relaxation); (ii) the widespread disagreement in regard to comparative measurements with acceleromyography *versus* MMG or electromyography (EMG); and (iii) the inherent variability resulting from the fact that 20 patients were enrolled at each of four different medical centres. Most importantly, complete equilibration (steady-state conditions) for the anaesthetic agents[10] and rapacuronium between the muscle and plasma compartments may not have been achieved during the 45–60 min study period.

In conclusion, when potent inhalation agents are administered in clinically relevant concentrations for maintenance of anaesthesia, the neuromuscular blocking activity, recovery profile and infusion requirements for rapacuronium (administered as a variable-rate infusion) were similar to those observed during a propofol-based anaesthetic technique. Further studies are needed to validate these results using other neuromuscular monitoring techniques, a more tightly controlled propofol infusion rate and fixed ET concentrations of the inhaled agents.

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Which is most pungent: isoflurane, sevoflurane or desflurane?

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We compared the pungency and tolerability of three inhaled anaesthetics in a randomized, double-blind study. Eighty-one unpremedicated patients (n=27, each group) inhaled 2 MAC of isoflurane (2.3%), desflurane (12%) or sevoflurane (4%) for 60 s from an anaesthetic breathing circuit via a mask. Two blinded observers recorded coughing, complaints of burning and irritation, and how long the inhalation was tolerated. One sevoflurane patient coughed, but completed the study period, whereas 11 isoflurane patients and 20 desflurane patients coughed, objected verbally or removed the mask forcefully. All sevoflurane, 20 isoflurane and seven desflurane patients completed the study period (average 60, 49 and 33 s, respectively, P<0.05). The irritability grading was: desflurane > isoflurane > sevoflurane (P<0.05). Sevoflurane is the least irritating agent for inhalation at 2 MAC concentration.

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Keywords: coughing; anaesthetics, volatile, isoflurane; anaesthetics, volatile, sevoflurane; potency, anaesthetic, MAC; potency, anaesthetic, tolerance

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Volatile anaesthetics vary in their pungency. This limits their use for induction of anaesthesia. We assessed the acceptability of equally potent (2 MAC) inhaled concentrations of three commonly used volatile anaesthetic vapours.

Materials and methods

Eighty-one male patients, requiring or requesting general anaesthesia for their surgical procedure, were included in this randomized, double-blind investigation, approved by the institutional review board. Patients with signs of active or severe pulmonary disease were excluded. Smoking was not an exclusion criterion, unless patients were coughing frequently or were wheezing. No pre-medication was given. Standard monitoring and an intravenous infusion of a crystalloid solution were started. A table of random numbers was used to assign the anaesthetic vapour. One investigator (M.I.G.) primed the anaesthetic circuit and 3-litre reservoir bag with vapour and oxygen. To confirm the 2 MAC concentration in the circuit, a Datex Capnomac gas-analyser was used in addition to the Ohmeda respiratory gas monitor. Priming was considered to be complete when vapour concentrations were identical in both analysers (4%, 2.3% and 12% for sevoflurane, isoflurane and desflurane, respectively) and remained constant for at least 1 min. Two observers (M.T. and C.H.) were at the patient's side, blinded to treatment, vaporizers and gas-analysers.

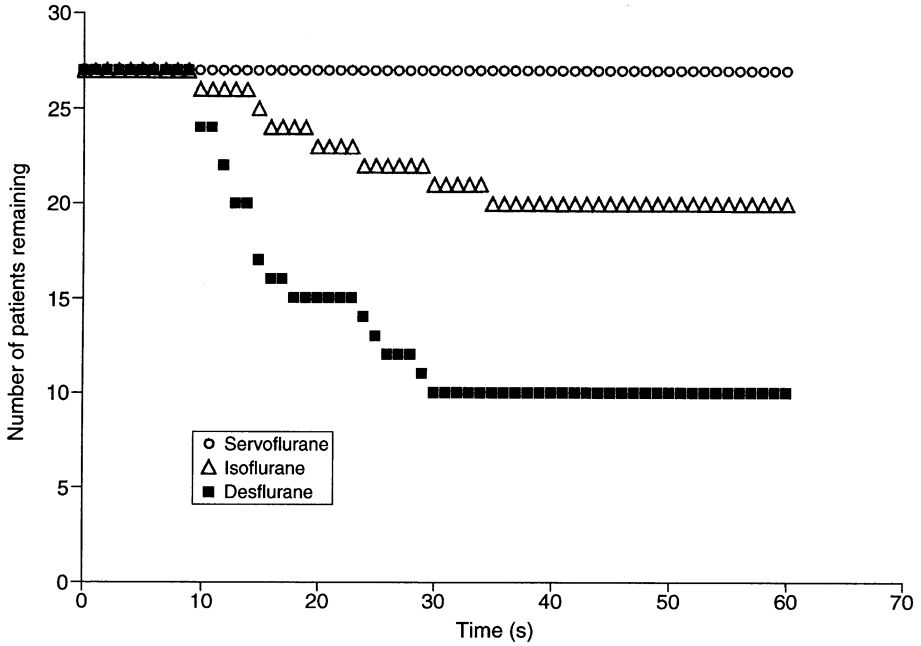

Fig 1 Patients who continue to breathe the anaesthetic versus time from the start of the inhalation.

To ensure a leak-proof fit during the study and prevent potential entrainment of room air during the study period, a facemask was firmly applied to the patient's face. The patient was then instructed to exhale forcefully while the chimney-piece on the mask was occluded. If an air-leak existed around the mask, it was adjusted until no leak could be detected and held in place throughout the 60-s inhalation.

A Fink non-rebreathing valve[1] was used in this study to ensure a constant inspired concentration throughout the study period. It was attached in series to a three-directional valve leading to either room air or to the primed breathing circuit. At the start of the 60-s study period, the three-way valve was turned and the patient was instructed to take a single deep breath followed by normal breathing. The observers looked for signs of irritation, such as coughing, head movement or forceful removal of the mask by the patient. During the study period, the patient was asked whether he could continue or wanted the mask removed. The duration of time the inhalation was tolerated was measured by a stopwatch (C.H.). The study period ended when the patient expressed unbearable irritation, removed the mask, or after 60 s.

Statistical analysis

The chi-squared test was used to compare the responses to the three vapours. Analysis of variance was used to compare the time-of-tolerance. When the *F*-test of the analysis of variance was statistically significant, Bonferroni multiple comparison procedure was performed. A *P*-value less than 0.05 was considered statistically significant.

Results

There were no obvious systematic differences between the patients in the groups. Because this study was performed at a Veterans Affairs Hospital, all patients were male. The number of smokers in each group was similar (13 in the desflurane group, 14 in the isoflurane group and 14 in the sevoflurane group). No patient had a history of symptoms of COPD, asthma or other pulmonary disease.

One sevoflurane patient, 11 isoflurane patients and 20 desflurane patients coughed or objected overtly to inhaling the gas mixture ($P<0.05$). When questioned about burning, irritation or other discomfort, none of the sevoflurane patients complained, while 12 isoflurane and 21 desflurane patients did ($P<0.05$).

With time (seconds) as a variable, the means in all groups were also significantly different when compared with each other ($P<0.05$). Figure 1 shows how long patients tolerated the inhalation and how many completed the 60-s study period.

No correlation could be found between smoking history and reaction to the inhalation.

Discussion

A novel approach to rapid induction by mask is the inhalation of a single deep breath of high concentration of potent vapour. This 'vital capacity breath technique' has been investigated comparing sevoflurane and isoflurane,[2,3] as well as with sevoflurane and halothane[4] in adults. Sevoflurane not only acted more rapidly, but also produced an induction with a lower incidence of coughing and 'better

patient acceptance'.[2 3 5] A different study compared the irritative qualities of four vapours at 1 and 2 MAC in volunteers.[6] Pungency was graded as isoflurane > enflurane > halothane > sevoflurane. Unfortunately, desflurane was not included in this comparison. It has the lowest blood–gas partition coefficient, but is associated with a high incidence of coughing and irritation.[7 8]

Our results show that during a 60-s inhalation of a 2 MAC concentration, sevoflurane is the least irritating anaesthetic agent. Isoflurane is more irritating than sevoflurane, but less so than desflurane, which seems to be unacceptably pungent. Most patients (20 out of 27) objected strongly to the inhalation.

A positive smoking history had no significant effect on the incidence of patient complaints. This may have been due to patient selection, as patients with respiratory symptoms were excluded from this study.

There are some limitations to our study. A 60-s time period was arbitrarily chosen, because we only sought to compare the initial irritability of the vapours. We think it is significant that some patients (seven receiving isoflurane, 20 receiving desflurane, respectively) did not tolerate even 60 s of exposure. We observed that very few patients lost consciousness after a single breath or within the 60-s time period. This needs further evaluation.

Second, the MAC concentration (and its multiple) represents equipotency based upon the response to a standardized surgical incision. It may not represent equipotency for airway irritability. Two MAC of desflurane should perhaps be compared with a higher concentration of isoflurane and sevoflurane. Equipotency in pungency remains conjectural.

Third, modern anaesthesia delivery systems use semi-closed circle systems, which may not be simulated exactly by a non-rebreathing valve. However, this valve allows delivery of only the anaesthetic mixture, the composition of which can be maintained precisely.[9 10] The purpose of its use was merely to deliver a constant anaesthetic concentration.

We conclude that, at the 2 MAC concentration, sevoflurane is significantly less irritating to the airways than isoflurane, and both are significantly less irritating than desflurane. Sevoflurane seems to be the best agent for rapid induction of general anaesthesia by mask.

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Water vapour in a closed anaesthesia circuit reduces degradation/ adsorption of halothane by dried soda lime

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Dry lime causes a loss of volatile anaesthetics by degrading and adsorbing them. Degradation produces toxic substances and heat. Rehydration of lime stops degradation. If humidified breathing gases rehydrate lime, closed anaesthesia-circuits may reduce the loss of anaesthetics. To test this hypothesis we ventilated a reservoir bag with PhysioFlex®-devices using fresh (F) and dried (D) soda lime both in the presence (+H) and absence (–H) of halothane. We measured halothane delivery, humidity, temperature, and lime weight. Halothane was lost for 13 min in D+H. Humidity increased steeper with fresh lime, whereas absorbent weight increased more with dried lime; halothane increased both variables (F+H: 99%, 8 g; F–H: 93%, 6 g; D+H: 58%, 17 g; D–H: 24%, 15 g). Surprisingly, temperature remained constant, probably because of the high gas flow (70 litres min^{-1}) generated inside the Physioflex®. These findings indicate rehydration of dried lime by humid gases and a rapid cessation of the loss of halothane in the PhysioFlex®.

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Fresh carbon dioxide absorbents (soda lime and Baralyme®) contain about 12–17% of water.[1 2] Various situations result in unnoticed drying of lime[2 3] which may be harmful since dried lime degrades volatile anaesthetics to toxic products (e.g. carbon monoxide).[1 2] Additionally, degradation produces heat that may be deleterious to the airways.[2] Rehydration of dried lime abolishes these effects.[1 2]

Humidification of breathing gases, which is best in closed-circuits may lead to fast rehydration of dried lime. Therefore, we hypothesized that the PhysioFlex® closed-circuit anaesthesia machine reduces degradation of volatile anaesthetics by dried soda lime. This machine generates a high gas flow inside the circuit to homogenize the gas components and to prevent rebreathing of expired gas.[4] This gas flow may promote heat transfer from the absorbent to the patient, increasing the risk of airway injury. We also tested if, as assumed elsewhere,[1] the degradation of halothane liberates water.

Methods and results

To study how the loss of halothane from the PhysioFlex® is influenced by the lime's water content, we used either fresh (F+H, n=4) or dried (D+H, n=4) soda lime (Draegersorb 800, Draeger, Lübeck, Germany). It was dried by passing oxygen (10 litres min^{-1}) through an absorbent-packed cylinder until the repeatedly measured weight (scale type 16410; Maul, Bad König, Germany) of the cylinder was constant. Then, an oxygen flow of 1 litres min^{-1} was used to keep the lime dry.

The PhysioFlex® has been described in detail previously.[4] It is a closed-circuit anaesthesia machine that delivers the chosen volatile anaesthetic with end-expiratory anaesthetic concentration as the feedback-controlled variable. (With feedback control of the inspiratory concentration the machine works as a semi-closed circuit. This would have been inappropriate for our purpose.) Whenever the anaesthetic concentration (measured by infrared spectroscopy) is lower than set, liquid anaesthetic is injected into the circuit. Thus, the amount of anaesthetic that is necessary to reach and maintain the set concentration can be quantified. Because degradation and adsorption of the volatile anaesthetic will increase anaesthetic delivery by lowering the measured anaesthetic concentrations,[3] we expected a difference in anaesthetic delivery between our F+H- and D+H-experiments, i.e. a loss of anaesthetic from the gaseous phase of the system. As the PhysioFlex® removes surplus volatile anaesthetic in a built-in charcoal filter, we removed the charcoal to avoid interference with our measurements.

The circuit was dried to 5–8% humidity during 2–3 h with siliceous earth, a strongly hygroscopic agent (Caesar & Lorentz, Hilden, Germany). From the start of the drying procedure until the end of each experiment, the PhysioFlex® ventilated a 3 litre reservoir bag (tidal volume 700 ml, respiratory rate 9 min^{-1}, positive end-expiratory pressure 0 cmH_2O, 30% oxygen in air).

After drying of the PhysioFlex®, we exchanged the siliceous earth with the absorbent sample to be studied without opening the circuit, took baseline measurements, and started carbon dioxide supply (200 ml min^{-1}). (The PhysioFlex® has two absorbent containers, one of which can be selectively bypassed. This allows the introduction of an absorbent sample without opening the circuit.) Carbon dioxide absorption contributes essentially to the rehydration of dried lime by producing water. Thereafter, we set an end-expiratory halothane concentration (Hal_{et}) of 2.0 vol% in the respective experiments and maintained this concentration until the end of the experiments (40 min). We measured continuously halothane delivery (PhysioFlex®), humidity, and temperature (Hygrotest 6200, Testotherm, Lenzkirch, Germany) inside the inspiratory limb of the circuit. Absorbent was weighed before and after each experiment.

All data are shown as median (range).

Substantial amounts of halothane were lost in the initial phase of the D+H experiments (stars in Fig. 1A). The median difference in the delivery of liquid halothane between D+H and F+H experiments was 1.96 ml after 6 min, peaked at 2.20 ml after 13 min and then decreased continuously to 1.59 ml. With D+H, the time to attain the set Hal_{et} was increased about 4-fold (D+H, 7 (6–9) min; F+H, 2 (1–2) min), the corresponding halothane dose was more than doubled (D+H, 3.9 (3.6–4.1) ml; F+H, 1.7 (1.2–1.7) ml) compared with F+H. However, to maintain Hal_{et} less halothane was delivered in the D+H experiments. Of note, the end of halothane loss coincided with humidity exceeding 20% during the D+H experiments. These findings indicate a substantial loss of halothane by dried lime in the initial minutes. However, about 30% (0.61 ml liquid halothane) of lost anaesthetic reappeared during the later course of the experiment.

These experiments were compared to experiments without halothane (F–H n=3; D–H, n=3) to determine if halothane influences the time course of the measured variables. The initial relative humidity and carbon dioxide supply was comparable in all experiments. We found considerable differences in the time course of humidity changes between the groups. Humidity increased steeply and approached 100% during the F experiments, whereas it remained below 70% (D+H) and 30% (D–H) after an initial decrease. The presence of halothane always accelerated humidification (Fig. 1B). The increase in absorbent weight was 17 (14–20) g for D+H, 15 (12–18) g for D–H, 8 (6–9) g for F+H and 6 (6–6) g for F–H. These results indicate that dried lime is rehydrated at the expense of humidification of the breathing gases and that water is liberated during degradation and/or adsorption of halothane. Temperature remained constant during all experiments.

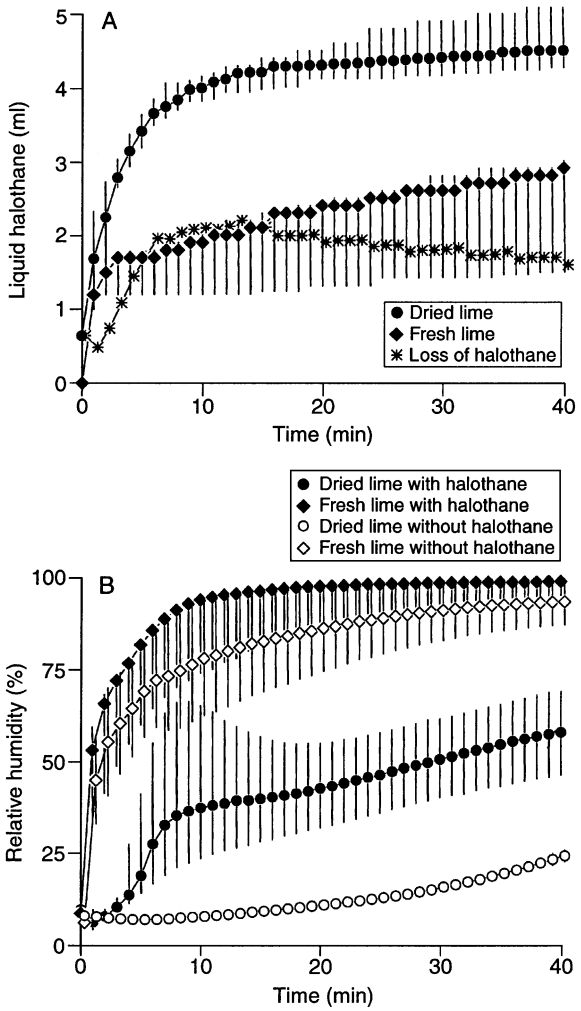

Fig 1 Time course of halothane delivery, loss of halothane and relative humidity inside the PhysioFlex®. Data presented as median (range). (A) Halothane delivery was considerably higher when dried lime (n=4) was used compared to fresh lime (n=4). The difference between fresh lime and dried lime experiments, i.e. the loss of halothane increased steeply during the first 6 min, peaked after 13 min and decreased again after this peak. (B) Relative humidity increased much steeper when fresh lime was used (halothane, n=4; without halothane, n=3) than during the experiments with dried lime (halothane, n=4; without halothane, n=3). Note that the increase of humidity was preceded by a small decrease at the beginning of the experiments with dried lime. The presence of halothane increased relative humidity compared to experiments without halothane.

Comments

We have shown for the first time that the loss of halothane caused by dried soda lime ceases rapidly in the PhysioFlex® and that dried lime is rehydrated at the expense of the humidification of the breathing gases. Although degradation of halothane produces heat, temperature inside the inspiratory limb did not increase.

The loss of halothane which resulted from degradation and adsorption by dried soda lime[1 2 5 6] decreased by 0.61 ml after the 13th minute of our experiments without reaching a plateau (Fig. 1A). Thus, at least 27% of the lost anaesthetic was not degraded. It was first adsorbed in the molecular sieve of the dried lime and then replaced by water that rehydrated the absorbent.[1 3] Rehydration of dried lime by water vapour is generally possible, as proven by the increasing absorbent weight and initially decreasing humidity in our D+H and D–H experiments. The loss of halothane ceased more rapidly when humidity exceeded 20% and an initial humidity of 20% prevented any loss of halothane in similar experiments (data not shown). Thus, a relative humidity of 20% inside the circuit seems to prevent degradation of halothane and this threshold is rapidly reached in the PhysioFlex®. Hence, for the PhysioFlex® we can contradict the assumption that water vapour may not suffice to rehydrate dried lime during a short period.[1]

The decreasing loss of halothane could be explained if halothane concentration was overestimated due to overlapping infrared spectra of halothane and its degradation products. However, with 1.3 vol% of halothane upstream of an absorber filled with dry soda lime, infrared spectroscopy failed to detect halothane downstream of this absorber for more than 10 min,[3] excluding overlapping spectra. Moreover, if we had used isoflurane or enflurane, overlapping spectra may have been feigned and anaesthetic delivery would have differed less, because these two anaesthetics are degraded only partially.[6] Therefore, halothane was the best choice for our experiments. (None of the PhysioFlex® used in this study contained sevoflurane or desflurane.)

As discussed above, the cessation of the loss of halothane indicates that the degradation and adsorption of halothane are reduced at this time. In a semi-closed anaesthesia circuit carbon dioxide production peaked 10–15 min after dried Baralyme® started to degrade desflurane.[5] This time point also indicates a reduction in anaesthetic degradation. Therefore, degradation seems to be reduced twice as fast in the PhysioFlex® than in semi-closed circuits. One possible reason for this is the faster humidification of breathing gases in closed compared to semi-closed circuits, resulting in faster rehydration of dried lime.

Temperature remained constant inside the inspiratory limb of the circuit during our experiments. Thus, although degradation of volatile anaesthetics excessively produces heat[2 3] and although heat transfer could be promoted by the high internal gas flow inside the PhysioFlex®,[4] thermal injury of the patient's airway is unlikely to occur with this device. This is likely to occur as a result of the high gas flow cooling the lime and interrupting the vicious circle of a heat-boostered exothermic reaction.[1]

Baralyme® also degrades volatile anaesthetics, but it was not used because the two limes contain similar amounts of alkali hydroxides—the crucial components for degradation of volatile anaesthetics—and no qualitative differences between the two limes have been reported concerning anaesthetic degradation.[1] Thus, our results may predict the situation with Baralyme®.

In conclusion, dried soda lime causes a loss of halothane that ceases rapidly within the PhysioFlex® because of rapid humidification of the dried lime. Furthermore, thermal injury of the patient's airway is unlikely to occur with this device.

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Randomized study of intravenous fluid preload before epidural analgesia during labour

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We performed a randomized controlled trial of the effect of intravenous fluid preload on maternal hypotension and fetal heart rate (FHR) changes in labour after the first epidural injection. Group 1 (49 women) received 1 litre of crystalloid preload. Group 2 (46 women) received no preload. No statistically significant difference was shown between the two groups for either of the outcomes. Hypotension was found in three women in group 1 and five in group 2 (P=0.4). Deterioration in FHR pattern was found in four women in group 1 and 11 in group 2 (P=0.08). This study has not shown a significant increase in the incidence of hypotension when intravenous preload is omitted before epidural analgesia using a low concentration of bupivacaine during labour. Because of the clinical importance of the difference in the rate of FHR deterioration between the two groups, we continue to administer preload for high-risk cases.

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In 1978, Collins and colleagues[1] demonstrated a significant reduction in maternal hypotension and fetal heart rate (FHR) changes when 1 litre of Hartmann's solution was given intravenously as a preload before epidural analgesia with bupivacaine 0.375%. Epidural analgesia is now usually initiated with weaker solutions of local anaesthetic, which may produce less hypotension, so preloading may be unnecessary. We have investigated this hypothesis.

Methods and results

The study was approved by the United Bristol Healthcare Trust Medical Ethics Committee. Healthy labouring women with a singleton cephalic fetus and cervical dilatation ⩽8 cm and requesting epidural analgesia were eligible. Women with hypertension, body mass >100 kg or fetal distress were excluded.

The size of the study was based on that of Collins and colleagues,[1] who studied 104 women. We recruited 100 women. Verbal consent for the study was gained after informing the women about epidural analgesia.

Intravenous access was obtained using a 14 G cannula. Allocation to one of two groups was determined on the basis of a computer-generated list. In group 1, 1 litre of Hartmann's solution was infused rapidly before the epidural test dose. In group 2, the infusion was run at the slowest possible speed.

The cuff of an automatic blood pressure instrument (Dinamap; Johnson & Johnson, Ascot, UK) was placed on the left arm, and two baseline readings of systolic and diastolic pressure were taken between uterine contractions with the subject in the left lateral position. FHR was monitored continuously with an external ultrasonic transducer and recorded on a paper printout.

Fifteen millilitres of 0.1 or 0.2% bupivacaine containing fentanyl 50 μg was used to achieve analgesia. Bupivacaine 0.1% was usually used if the cervical dilatation was less than 5 cm, otherwise the 0.2% concentration was given. When the epidural catheter was in place, a test dose of either 8 ml of 0.1% or 4 ml of 0.2% solution was given. If there were no adverse effects after 5 min, the remainder of the 15 ml was injected. Blood pressure was measured between uterine contractions every 5 min for 30 min after the test

Table 1 Hypotension and FHR changes after epidural compared with before the block was established. No significant differences were found when comparing group 1 *versus* group 2 or bupivacaine 0.1 *versus* 0.2%. (NB. If the FHR was abnormal before the epidural and after it, this would be registered as no change)

	Group 1: preload			Group 2: no preload		
Bupivacaine	**0.1%**	**0.2%**	**All**	**0.1%**	**0.2%**	**All**
No hypotension	31	15	46	24	17	41
Hypotension	2	1	3	3	2	5
Total	33	16	49	27	19	46
FHR						
Improved	0	0	0	1	0	1
No change	24	8	32	16	8	24
Deteriorated	2	2	4	7	4	11
Total	26	10	36	24	12	36

dose. If the woman turned over during this period, the blood-pressure cuff was transferred to the dependent arm.[2]

Hypotension was defined as a decrease, in the 30 min after the test dose, of greater than 20% from the lowest baseline systolic pressure. The baseline FHR trace was defined as the 30 min before the test dose, and FHR was then recorded for 60 min after the test dose. Traces were analysed and classified as normal, suspicious or abnormal, according to the scheme proposed by Steer and Danielian,[3] by an obstetrician (MSM) blinded to whether the patient had received preload.

Statistical analysis was performed using the Mann–Whitney test, the chi-squared test, Fisher's exact test or the *t*-test to compare physical and obstetric characteristics, the concentration of bupivacaine used, blood pressure changes and the FHR pattern. A probability of $P<0.05$ was taken as statistically significant.

Of the 100 women recruited, 51 were assigned to the preload group and 49 to the no-preload group. One woman from each group was excluded during the study. One had a placental abruption and Caesarean section, and the other delivered vaginally. One woman in group 1 and two in group 2 were excluded after completion of the study, as they were found to have had abnormal baseline FHR patterns before the epidural. Analysis was performed on a total of 49 women in the preload group and 46 in the no-preload group.

There was no difference in age, height, weight, parity and cervical dilation between the two groups. Hypotension occurred in three women in group 1 and five women in group 2 (Table 1; $P=0.4$). Hypotension was treated easily in all except for one woman in group 2. She had several episodes of hypotension for the first 40 min after starting the epidural despite treatment with 1.5 litre of Hartmann's solution and ephedrine 15 mg.

After the epidural, in group 1 the FHR pattern was normal in 32 women, suspicious in eight women and abnormal in one woman; in group 2 the FHR pattern was normal in 24 women, suspicious in 14 and abnormal in two. There were no differences between the two groups with respect to the number of parturients with suspicious or abnormal traces after the epidural ($P=0.21$).

FHR data were also investigated to detect any change from before to after the epidural. Deterioration occurred if a normal trace became suspicious or abnormal, or if a suspicious trace became abnormal. Data from both before and after the epidural were available for only 72 women. There was no statistically significant difference between the two groups in FHR deterioration (Table 1; $P=0.08$).

Hypotension and FHR deterioration occurred with similar frequencies in women who received 0.1 or 0.2% bupivacaine.

Discussion

Collins and colleagues showed a 2% incidence of hypotension in women who had a 1-litre preload versus 28% in a no-preload control group ($P=0.005$).[1] Using the same definition, we found hypotension in 6% of women who had a 1-litre preload and 10% of women with no preload. The difference between groups was not statistically significant. Although the investigator was not blinded as to which group the woman belonged to, the use of automated blood pressure recording in our study minimized observer bias.

A power analysis of our results showed that 1530 women would have had to be included in a study to determine whether preloading reduces hypotension, with a power of 0.9 and significance level of 0.05. Given that hypotension is infrequent, usually not severe and easily treated, such a study does not seem to be indicated.

Collins and colleagues[1] demonstrated a significant protective effect of preloading on the risk of FHR abnormalities after epidural. These occurred in 12% of preloaded women *versus* 34% with no preload. We did not show a statistically significant increase in the risk of a deterioration in FHR pattern when preloading was omitted. However, our proportion of cases (11 and 30%) was similar to that of Collins and colleagues.[1] Twenty-three women had FHR traces that were inadequate for interpretation, reducing the power of our trial to demonstrate a significant difference between the two groups. On the basis of our results, we would have to study 200 women to demonstrate a real difference in FHR deterioration with a power of 0.9 and significance of 0.05.

Early studies suggested a link between maternal hypotension after the use of labour epidurals and FHR abnormalities, but women were managed supine, leading to aortocaval compression.[4 5] More recently, Collins and colleagues[1] and Palmer and colleagues[6] did not find a relationship between hypotension and FHR abnormalities. Only one of the women in the present study who developed hypotension had a worsening FHR pattern.

The manner in which preloading might protect against FHR changes is not clear. Steiger and Nageotte[7] found that an increase in uterine baseline tone and contraction frequency after epidural analgesia, rather than hypotension, was associated with subsequent FHR abnormalities. As Cheek and colleagues[8] demonstrated a reduction in uterine contraction frequency after a 1-litre preload, the administration of a preload might balance a tendency towards an increase in contractility of the uterus after regional analgesia.

The clinical importance of the majority of FHR changes after epidural block is also uncertain. Although the method of FHR analysis used by Collins and colleagues[1] is not directly comparable with that which we used,[3] very few cases from either group in their study had unquestionably pathological features. We found only one abnormal trace in our preload group and two in the no-preload group. Spencer and colleagues[9] noted that the use of epidural analgesia was associated with an increased rate of FHR abnormalities, but not with fetal acidosis.

In summary, we found that omitting intravenous fluid loading before epidural analgesia in normotensive labouring women did not increase the incidence of hypotension significantly compared with women given a 1-litre preload. However, fluid administration before epidural may protect against FHR deterioration, possibly through a transient tocolytic action. Until further data are available, we suggest that intravenous preloading is used before epidural analgesia in labour when there is suspected or actual fetal compromise.

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Prospective evaluation of deep topical fornix nerve block *versus* peribulbar nerve block in patients undergoing cataract surgery using phacoemulsification

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We compared the efficacy of deep topical fornix nerve block anaesthesia (DTFNBA) *versus* peribulbar nerve block in patients undergoing cataract surgery using phacoemulsification. We studied 120 patients, allocated randomly to two groups. Group 1 (n=60) received peribulbar block with 5 ml of a 1:1 mixture of 0.5% plain bupivacaine and 2% lidocaine supplemented with hyaluronidase 300 i.u. ml^{-1}. Group 2 received DTFNBA with placement of a sponge soaked with 0.5% bupivacaine deep into the conjunctival fornices for 15 min. No sedation was given to either group. Analgesia was assessed by the reaction to insertion of the superior rectus suture and by questioning during the procedure. A three-point scoring system was used (no pain=0, discomfort=1, pain=2). Scoring was repeated at keratotomy, hydrodissection and hydrodelineation, phacoemulsification, irrigation and aspiration, and at intraocular lens insertion. If the patient's pain score was 0 or 1, no further action was taken. If the pain score at any stage of the operation was 2, intracameral injection of 1% preservative-free lidocaine was given. One patient in Group 2 needed intracameral lidocaine at the stage of phacoemulsification (P>0.05) and four experienced discomfort at irrigation and aspiration (P=0.043). We conclude that DTFNBA may be a useful needle-free anaesthetic technique in patients undergoing cataract surgery using phacoemulsification.

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General anaesthesia is hazardous in a large number of patients undergoing ophthalmic surgery, as many of them are elderly with multisystem disease. For diabetic patients, local anaesthesia is preferable as it reduces, to a great extent, the endocrine response to surgery.[1] Peribulbar block is becoming increasingly popular, as it is safer than retrobulbar block.[2] However, insertion of a needle near the eye is associated with the necessity to stop anticoagulant therapy, introduces the risk of retrobulbar bleeding and potential perforation of the globe. Such risks may necessitate the use of topical anaesthesia, although this is unusual. The use of deep topical fornix-applied nerve block anaesthesia has been reported in cataract surgery by Rosenthal.[3] It involves placement of local anaesthetic into the conjunctival fornices, from which the local anaesthetic diffuses across the conjunctiva into the peribulbar space and into the scleral nerves behind the eyes. In this study, we compared deep topical fornix nerve block anaesthesia (DTFNBA) with peribulbar nerve block in patients undergoing cataract surgery using phacoemulsification.

Methods and results

One hundred and twenty patients scheduled for elective intraocular surgery were enrolled in the study after we had obtained approval from the institutional ethics committee and patient consent. All patients had been assessed as suitable for a regional block technique and were unpremedicated. Patients were allocated randomly to one of two groups (closed envelope method). Group 1 (n=60) received peribulbar block. Group 2 (n=60) received DTFNBA.[3] The axial length (the distance from the cornea to the retina) is usually measured as part of the ophthalmic assessment using the axial length scanner. If the axial length is 26 mm or longer, the globe is elongated.[4] These patients were omitted from the study, as the risk of globe perforation if peribulbar block is used is greater.

Before the block, a peripheral vein was cannulated and heart rate, oxygen saturation and non-invasive arterial blood pressure were monitored. In both groups, the conjunctival fornices were anaesthetized with local anaesthetic drops (oxybuprocaine 0.4%) before the block was started.

Peribulbar block was performed with a 5 ml syringe and a 25 gauge, 25 mm long disposable needle using a single inferotemporal injection[5 6] with 5 ml of a 1:1 mixture of 0.5% plain bupivacaine and 2% plain lidocaine supplemented with hyaluronidase 300 i.u. ml^{-1}. With the gaze fixed straight ahead in the primary position, the injection site was identified at the junction of the lateral one-third and medial two-thirds of the inferior orbital rim. The direction of the needle was slightly medial and cephalad. The local anaesthetic was injected slowly over a period of 1 min. DTFNBA was performed using two sponges (2×3 cm) soaked with 0.5% bupivacaine, applied deep into the conjunctival fornices.[3] The sponges were removed after 15 min. The surface anaesthetic effect was tested by grasping the limbus with Castroviejo 0.12 tissue forceps. A simple pain scoring system was used: no pain=0, discomfort=1, pain=2. The scoring was done at different stages of surgery: insertion of the superior rectus suture; keratotomy; hydrodissection and hydrodelineation; phacoemulsification; irrigation and aspiration; and intraocular lens insertion. If the pain score was 0 or 1, no further management was required. If the pain score was 2 at any stage of the operation, intracameral injection of 1% preservative-free lidocaine was given.

Parametric data were analysed using Student's *t*-test; non-parametric data were compared using the Mann–Whitney test. A P value of <0.05 was considered statistically significant.

There was no significant difference between the patient characteristics of the two groups (Table 1).

In Group 1, no patient experienced discomfort or pain at any stage of the operation. In Group 2, one patient experienced discomfort at the superior rectus suture, keratotomy, hydrodissection and hydrodelineation and phacoemulsification ($P>0.05$), and four patients experienced discomfort at irrigation and aspiration ($P=0.043$). At the stage of intraocular lens insertion, three patients in Group 2 experienced discomfort ($P>0.05$). In the only patient who experienced pain at the time of phacoemulsification, intracameral injection of 1% preservative-free lidocaine was applied.

The numbers of patients in each group with different pain scores at each stage of surgery are shown in Table 2.

Comment

Peribulbar block has gained popularity over the last few years, as it is safer than the traditional retrobulbar block.[2 4] In peribulbar block the needle tip remains outside the muscle cone, and thus the complications of retrobulbar block are avoided. However, peribulbar block has its own complications. Brain stem anaesthesia resulting from subarachnoid injection can occur if the peribulbar needle is inadvertently placed in the retrobulbar space. This is unlikely with a 25 gauge, 25 mm long needle. Extraocular muscle paresis can occur if local anaesthetic is injected directly into the muscle, or the needle may puncture a superficial vessel, causing conjunctival haemorrhage. The incidence of scleral perforation is higher with retrobulbar blocks. However, it has been reported with peribulbar block, especially if the axial length is more than 26 mm.[4] These

Table 1 Patient characteristics. Values are mean (SD) and age, range

	Group 1 Peribulbar block	**Group 2 DTFNBA**
Men/women	20/40	15/45
Age (yr)	74 (00–00)	75 (00–00)
Weight (kg)	64 (11.4)	60 (10.8)
ASA I	10	9
ASA II	30	31
ASA III	20	20

Table 2 Numbers of patients in relation to pain score at different stages of the operation. Data were analysed using the Mann–Whitney test. *P = 0.043 between groups

	Group 1 Peribulbar block			**Group 2 DTFNBA**		
	No pain	**Discomfort**	**Pain**	**No pain**	**Discomfort**	**Pain**
Superior rectus suture	60	0	0	59	1	0
Keratotomy	60	0	0	59	1	0
Hydrodissection and hydrodelineation	60	0	0	59	1	0
Phacoemulsification	60	0	0	58	1	1
Irrigation and aspiration	60	0	0	56	4*	0
Intraocular lens insertion	60	0	0	57	3	0

complications are avoided with the use of DTFNBA, yet a good quality of analgesia is maintained. Rosenthal[3] has postulated that placement of local anaesthetic into the fornices allows absorption by the nerve trunks subserving the conjunctiva as they radiate across it. At the same time, by being absorbed posteriorly into the peribulbar space (and possibly transconally into the retrobulbar space), the posterior ciliary nerves, which supply the anterior sclera, anterior conjunctiva and limbus as well as the iris and ciliary body, are anaesthetized at their nerve roots.[3]

Each time a needle is introduced into the orbit there is a small but definite risk of complications. In this study, it has been shown that the use of DTFNBA offers analgesia comparable to that given by peribulbar block. Additional local analgesia may be required during lens irrigation and aspiration as there is significant patient discomfort at this stage of surgery. However, there is no akinesia with DTFNBA. This method is therefore not suitable for cataract surgery using extracapsular lens extraction; it is suitable only for surgery using phacoemulsification. The surgeon must be experienced with this type of surgery, as surgery is more difficult without akinesia. We conclude that DTFNBA is suitable for patients on anticoagulants and those who will not accept the use of injections around the eye. We recommend DTFNBA for patients undergoing cataract surgery using phacoemulsification.

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