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Low-dose sufentanil and lidocaine supplementation of general anaesthesia

This randomized double-blind study compared the effects of: (1) saline infusion (C); (2) sufentanil alone ($1.0 \mu\text{g} \cdot \text{kg}^{-1}$) (S); and (3) low-dose sufentanil ($0.5 \mu\text{g} \cdot \text{kg}^{-1}$) in combination with lidocaine ($1.5 \text{mg} \cdot \text{kg}^{-1}$) (LS); on the cardiovascular responses to tracheal intubation and on postoperative ventilation as monitored by respiratory inductive plethysmography in day-care surgical procedures of approximately 60 min duration. Thirty healthy, unpremedicated patients were studied. Thiopentone requirements were reduced by 40 and 28 per cent in the S and LS groups respectively compared with control ($P < 0.001$). Both treatments suppressed HR and BP responses ($P < 0.005$) to intubation. Postoperatively, PaCO_2 was elevated ($P < 0.05$) in group S. Dose-related respiratory depression was observed. The incidence of postoperative apnoea was significantly higher in both S and LS groups than compared with control ($P < 0.05$). However, only patients in group S showed higher apnoea index and mean apnoea duration over the initial 10–20 min after surgery compared with control ($P < 0.005$). In addition, group S showed slower respiratory frequency and prolonged expiratory time ($P < 0.005$). In conclusion, an induction dose of sufentanil ($1 \mu\text{g} \cdot \text{kg}^{-1}$) used in balanced anaesthesia of less than 70 min duration was associated with significant respiratory depression, particularly during the initial 10–20 min after

surgery, whereas low-dose sufentanil ($0.5 \mu\text{g} \cdot \text{kg}^{-1}$) with lidocaine ($1.5 \text{mg} \cdot \text{kg}^{-1}$) had minimal postoperative respiratory depression and comparable attenuation of pressor responses to intubation.

Cette étude randomisée à double-insu a comparé les effets de: (1) la perfusion de salin (C); (2) le sufentanil seul ($1,0 \mu\text{g} \cdot \text{kg}^{-1}$) (S); et (3) une petite dose de sufentanil ($0,5 \mu\text{g} \cdot \text{kg}^{-1}$) en combinaison avec la lidocaïne ($1,5 \text{mg} \cdot \text{kg}^{-1}$) (LS); sur les réponses cardiovasculaires à l'intubation trachéale et la ventilation postopératoire telle qu'étudiée par pléthysmographie inductive pour une durée de 60 minutes. Trente patients en bonne santé, non prémédiqués ont été étudiés. Les doses de thiopentone ont été diminuées de 40 et 28 pour cent respectivement dans les groupes S et LS comparativement au contrôle ($P < 0,001$). Les deux régimes ont diminué la réponse de l'intubation sur la fréquence cardiaque et la tension artérielle ($P < 0,005$). En période postopératoire la PaCO_2 était élevée ($P < 0,05$) dans le groupe S. Une dépression respiratoire dépendant de la dose a été observée. L'incidence d'apnée postopératoire a été significativement plus élevée dans le groupe S et LS comparativement au contrôle ($P < 0,05$). Cependant seulement les patients du groupe S ont démontré un indice d'apnée supérieur et une durée d'apnée moyenne après chirurgie comparativement au contrôle ($P < 0,005$). En plus le groupe S a démontré une fréquence respiratoire plus basse et un temps d'expiration prolongé ($P < 0,005$). En conclusion, une dose d'induction de sufentanil ($1 \mu\text{g} \cdot \text{kg}^{-1}$) utilisée pour une anesthésie balancée d'une durée inférieure à 70 minutes est associée à une dépression respiratoire significative, particulièrement durant le temps initial de 10 à 20 minutes après la chirurgie. Une dose moindre ($0,5 \mu\text{g} \cdot \text{kg}^{-1}$) de sufentanil et de lidocaïne ($1,5 \text{mg} \cdot \text{kg}^{-1}$) a présenté une dépression respiratoire minime en période postopératoire et une atténuation comparable de la réponse à l'intubation.

Key words

ANAESTHESIA: general, outpatient;

ANALGESICS: sufentanil;

MONITORING: ventilation, respiratory inductive plethysmography, vascular.

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Sufentanil,¹ an analogue of fentanyl, is five to ten times more potent, has a more rapid onset of action,² is more effective in preventing intraoperative hypertension and tachycardia,^{2–4} and results in less cumulative respiratory depression^{5,6} than the parent compound. However, numerous cases of respiratory depression or arrest have been

reported with sufentanil.⁷⁻¹¹ Nonetheless, no detailed analysis of postoperative respiratory depression by sufentanil has been undertaken. With growing popularity in ambulatory care, relatively longer duration of surgery is being performed in outpatient settings and in patients with stable, complex diseases. The balance between detrimental cardiovascular responses¹²⁻¹⁴ to intubation and postoperative respiratory depression in the use of sufentanil in these surgical procedures has not been examined. Having shown that the cardiovascular response can be blunted by intravenous lidocaine prior to tracheal intubation,¹⁵ we sought to test the hypothesis that low-dose sufentanil in combination with lidocaine provided as stable a cardiovascular response to tracheal intubation and less postoperative respiratory depression than the recommended dose of sufentanil alone in a double-blind study in patients undergoing outpatient surgery lasting about 60 min.

Methods

Human Experimentation Committee approval and informed consent were obtained. Thirty patients from the Short Stay Unit, aged 18-60 yr, of ASA physical status I-II and with no pre-existing cardiac or respiratory disease, undergoing elective surgical procedures that required tracheal intubation were studied. Surgical procedures that involved the thorax or abdomen were excluded.

No preoperative sedation was given. Flow-volume spirometry (570 Wedge, Med. Science Electronics, Inc., St. Louis, MO) and respiratory inductive plethysmographic calibration (Respirace®, Ambulatory Monitoring, Inc., Ardsley, NY) were performed before surgery. Patients were randomly allocated into three groups: control (C); lidocaine ($1.5 \text{ mg} \cdot \text{kg}^{-1}$) with sufentanil ($0.5 \mu\text{g} \cdot \text{kg}^{-1}$) (LS) and sufentanil alone ($1.0 \mu\text{g} \cdot \text{kg}^{-1}$) (S). All patients were given 0.5 L crystalloid during the pre-oxygenation period. Baseline data were collected after five minutes of pre-oxygenation (time, -5 min), then precurarization of d-tubocurarine $0.05 \text{ mg} \cdot \text{kg}^{-1}$ was given. At time -3 min, either normal saline or lidocaine $1.5 \text{ mg} \cdot \text{kg}^{-1}$ was injected, followed by normal saline or sufentanil (0.5 or $1.0 \mu\text{g} \cdot \text{kg}^{-1}$). At time -2 min, thiopentone was titrated in 50 mg increments until loss of consciousness, as defined by loss of response to verbal command and loss of the eyelid reflex, assessed every 15 sec by two investigators during the induction of anaesthesia. Muscle relaxation was induced with succinylcholine $1.5 \text{ mg} \cdot \text{kg}^{-1}$. At Time 0, tracheal intubation was accomplished by the investigator within 20 sec. Controlled ventilation with 70 per cent nitrous oxide and 30 per cent oxygen was initiated. For the next five minutes, the patient was not surgically stimulated to allow haemodynamic measurements. Dosage of thiopentone used for induction was compared among groups.

Heart rate (HR), systolic (SBP) and diastolic blood pressures (DBP) were recorded by an automatic blood pressure cuff (Datascop®) at: Time -5 min (baseline), -4 min (precuarization), -3 min (study drug), -2 min (thiopentone), -1 min, 0 (laryngoscopy and intubation) and post-intubation every minute for five minutes. Atropine 0.6 mg IV was administered to patients if the HR was less than 50 bpm during continuous ECG monitoring.

Anaesthesia was maintained with 70 per cent nitrous oxide and 30 per cent oxygen, supplemented with vecuronium to maintain muscle relaxation as monitored with a nerve stimulator. Isoflurane was added to maintain the blood pressure within 20 per cent of the preoperative level. Ventilation was controlled to maintain the end-tidal PCO_2 at 35-40 mmHg. No additional doses of an opioid were given intraoperatively. At the end of the surgical procedure, neuromuscular blockade was reversed with neostigmine and glycopyrrolate and confirmed with train-of-four stimulation. The patients' tracheas were extubated in the operating room when they were awake, breathing spontaneously, and able to sustain head lift and strong hand grasp. The end-expiratory concentration of isoflurane was zero in all patients as monitored by mass spectrometry (Perkin Elmer) at the time of extubation. Extubation was accomplished within five minutes of the completion of surgery.

Details of the DC-coupled respitrace have been published¹⁶ and its accuracy has been confirmed in a variety of settings.¹⁷⁻¹⁹ Respiratory Inductive Plethysmograph (RIP) consists of two coils of teflon-insulated wire which are placed around the rib cage and abdomen to measure its cross-sectional area. This produces a proportional change in self-inductance of that coil which is related to lung volume. The RIP is not sensitive to changes in body position, and a single calibration with a spirometer by changing body position from the upright to the supine position is valid over a wide range of body positions.^{16,17} Calibration factors were calculated by the simultaneous equations method using the mean of two resting tidal breaths from the tidal volume record. Validation of correct calibration was obtained by measuring tidal volume (VT) simultaneously with RIP and spirometer during 20 seconds rebreathing from the spirometer. If the mean VT, calculated from RIP as the sum of rib-cage and abdominal contributions was greater than ± 10 per cent from the mean VT measured spirometrically, the inductance coils were re-applied and the calibration procedure repeated until the difference was less than ten per cent or the patient was excluded from the study.

The ventilatory pattern was monitored by RIP for ten minutes preoperatively and postoperatively at 10-20 min, 30-40 min and 50-60 min intervals after extubation. Analogue RIP signals were digitized at 20 Hz and data

were collected on microcomputer diskette as well as on a multichannel strip chart recorder for subsequent analysis. Breath detection software allowed breath-by-breath measurement or calculation of the following variables: respiratory frequency (F), inspiratory time (TI), expiratory time (TE), tidal volume (VT), mean inspiratory flow rate (VT/TI), minute ventilation ($\dot{V}_E$) and percentage of rib cage or abdominal contribution to VT. Apnoeas were defined as expiratory pauses of greater than ten seconds during which no tidal volume effort was discernible or the VT was less than 100 ml. The apnoea index was defined by the number of apnoeas per hour as expressed during the three ten-minute periods after extubation. All patients received 28 per cent oxygen by facemask and haemoglobin saturation was monitored by pulse oximetry. Naloxone 0.2 mg IV was only given to patients with prolonged apnoea that was accompanied by arterial desaturation, i.e., less than 90 per cent. Arterial blood gas analyses were performed at 30 min after surgery. Postoperatively, morphine IV was given for pain as needed by the recovery room nurses after the respirator was attached to the patients.

Data were expressed as mean $\pm$ SEM. Statistical analysis was done by a one-way ANOVA and was followed by Scheffe's multiple range test during post-hoc analysis of significant overall F's from the one-way ANOVA. The effect of time and group difference were correlated with repeated measures analysis of variance. Due to multiple comparisons, Bonferroni's adjustment for the level of significance was applied.

Results

Thirty healthy patients from the Short Stay Unit were studied with ten in each group. There were no differences among the three groups in age, weight or duration of anaesthesia and surgery (Table I). The thiopentone dose requirement was significantly lower in the LS and S groups than in the control group. When active treatment groups were compared, thiopentone requirements were significantly lower in the S than the LS group (Table II).

Heart rate (HR) in the control group was significantly increased above baseline at intubation and at two minutes following intubation. The mean HR in the LS and S groups changed minimally from baseline and was signifi-

FIGURE 1 Comparison of heart rate among control (C), lidocaine-sufentanil (LS) and sufentanil (S) groups over time. Baseline (-5 min), precurarization (-4 min), study drug (-3 min), thiopental (-2 min) and intubation (0 min) (mean $\pm$ SEM).

cantly lower than in the control group post-intubation (Figure 1). Systolic (SBP) and diastolic blood pressures (DBP) showed similar response profiles and were elevated markedly at one minute post-intubation in the control group. In contrast, SBP and DBP in the LS and S groups did not increase from baseline and were significantly lower than control group post-intubation (Figures 2 and 3). One patient in each LS and S group required intravenous atropine 0.6 mg post-intubation because of bradycardia (HR < 50 bpm).

Postoperatively, the arterial oxygen saturation was not significantly different among the three groups, ranging from 98–99 per cent. However, PaCO_2 was significantly elevated in the S group (Table II). One patient in group S exhibited a PaCO_2 of 69 mmHg and SaO_2 of 97 per cent at 30 min postoperation, with spontaneous improvement to 56 and 48 mmHg at 60 and 90 min respectively. No

TABLE I Comparison of demographic data

n	C 10	LS 10	S 10
Age (yr)	33 $\pm$ 4	38 $\pm$ 3	27 $\pm$ 2
Body weight (kg)	73.3 $\pm$ 5.0	70.1 $\pm$ 3.3	70.6 $\pm$ 3.5
Height (cm)	168 $\pm$ 2	169 $\pm$ 2	170 $\pm$ 3
Surgery (min)	70.8 $\pm$ 8.2	74.8 $\pm$ 8.2	67.1 $\pm$ 8.8

TABLE II Comparison of thiopentone requirement and postoperative arterial oxygen saturation and carbon dioxide tension

n	C 10	LS 10	S 10
Thiopentone (mg $\cdot$ kg ⁻¹)	5.0 $\pm$ 0.2	3.6 $\pm$ 0.2*	3.0 $\pm$ 0.2*†
SaO ₂ (%)	99 $\pm$ 1	99 $\pm$ 1	99 $\pm$ 1
PaCO ₂ (mmHg)	40.4 $\pm$ 1.7	45.5 $\pm$ 2.0	50.0 $\pm$ 3.1‡

Mean $\pm$ SEM

*P < 0.001 vs C.

†P < 0.05 vs LS.

‡P < 0.05 vs C.

FIGURE 2 Comparison of systolic blood pressure among control (C), lidocaine-sufentanil (LS) and sufentanil (S) groups over time. Baseline (-5 min), precurarization (-4 min), study drug (-3 min), thiopentone (-2 min) and intubation (0 min) (mean $\pm$ SEM).

FIGURE 3 Comparison of diastolic blood pressure among control (C), lidocaine-sufentanil (LS) and sufentanil (S) groups over time. Baseline (-5 min), precurarization (-4 min), study drug (-3 min), thiopentone (-2 min) and intubation (0 min) (mean $\pm$ SEM).

postoperative analgesia was required by this patient. Postoperative ventilatory patterns were significantly different among the treatment groups. The number of patients exhibiting apnoeas was also higher ($P < 0.05$) in LS and S groups (6/10 and 8/10 patients, respectively) versus control (1/8 patients). The highest apnoea index (number of apnoeas $\cdot$ hr $^{-1}$) was seen in the S group at 10–20 min postoperation; this value was significantly higher

FIGURE 4 Apnoea index (mean $\pm$ SEM) among the three groups at different time intervals after operation.

FIGURE 5 Apnoea duration (mean $\pm$ SEM) among patients with apnoea in the three groups at different time intervals after operation.

than in control and LS groups (Figure 4). Among patients with apnoeas, the mean apnoea duration showed a dose-response relationship to sufentanil particularly during the earliest postoperative monitoring period ($P < 0.005$) (Figure 5). Ventilatory pattern variables are summarized in Table III for pre- and postoperative monitoring periods. For technical reasons, data were incomplete for two control subjects and data are shown for eight control subjects. At ten minutes postoperatively, respiratory frequency (F) was significantly lower and expiratory time (TE) significantly longer in the S group compared with baseline and compared with the control and LS groups.

More patients tended to require postoperative analgesia in the control (40 per cent) than in the LS (20 per cent) and

TABLE III Detailed comparisons of ventilation variables by respiratory inductive plethysmography

	C (n = 8)	LS (n = 10)	S (n = 10)
Frequency (F) (breaths per minute)			
Baseline	15 ± 1	16 ± 1	15 ± 1
Postop 10–20 min	16 ± 1	13 ± 1	10 ± 1*
Postop 30–40 min	15 ± 1	13 ± 1	13 ± 1
Postop 50–60 min	15 ± 1	13 ± 1	14 ± 1
Inspiratory time (TI) sec			
Baseline	1.7 ± 0.2	1.6 ± 0.2	1.9 ± 0.2
Postop 10–20 min	1.6 ± 0.1	1.8 ± 0.1	1.8 ± 0.1
Postop 30–40 min	1.7 ± 0.1	1.7 ± 0.1	1.7 ± 0.1
Postop 50–60 min	1.6 ± 0.1	1.7 ± 0.1	1.6 ± 0.1
Expiratory time (TE) sec			
Baseline	2.5 ± 0.3	2.4 ± 0.3	2.6 ± 0.3
Postop 10–20 min	2.7 ± 0.8	4.1 ± 0.8	6.6 ± 0.8†
Postop 30–40 min	2.8 ± 0.6	4.2 ± 0.5	4.2 ± 0.6
Postop 50–60 min	2.8 ± 0.5	4.0 ± 0.4	4.1 ± 0.5
Tidal volume (VT) L			
Baseline	0.50 ± 0.07	0.48 ± 0.07	0.61 ± 0.06
Postop 10–20 min	0.57 ± 0.07	0.56 ± 0.06	0.67 ± 0.06
Postop 30–40 min	0.58 ± 0.06	0.56 ± 0.05	0.63 ± 0.06
Postop 50–60 min	0.48 ± 0.06	0.53 ± 0.05	0.58 ± 0.05
Minute ventilation per wt ($\dot{V}_E$ kg ⁻¹) (ml · min ⁻¹ · kg ⁻¹)			
Baseline	0.09 ± 0.01	0.11 ± 0.01	0.12 ± 0.01
Postop 10–20 min	0.11 ± 0.02	0.10 ± 0.02	0.10 ± 0.02
Postop 30–40 min	0.11 ± 0.02	0.10 ± 0.02	0.12 ± 0.02
Postop 50–60 min	0.09 ± 0.02	0.10 ± 0.01	0.11 ± 0.02
Respiratory drive (VT/TI) (litre · sec ⁻¹)			
Baseline	0.29 ± 0.03	0.30 ± 0.03	0.33 ± 0.03
Postop 10–10 min	0.37 ± 0.06	0.32 ± 0.05	0.39 ± 0.05
Postop 30–40 min	0.36 ± 0.05	0.34 ± 0.04	0.41 ± 0.04
Postop 50–60 min	0.31 ± 0.03	0.32 ± 0.02	0.37 ± 0.03
% Rib ventilation			
Baseline	38.6 ± 8.6	47.9 ± 8.6	51.4 ± 8.1
Postop 10–20 min	56.3 ± 6.2	63.4 ± 5.6	56.8 ± 5.6
Postop 30–40 min	52.8 ± 6.6	62.4 ± 5.9	55.7 ± 6.3
Postop 50–60 min	47.0 ± 6.5	58.4 ± 5.5	56.9 ± 6.1
% Abdomen ventilation			
Baseline	61.4 ± 8.6	52.1 ± 8.6	48.6 ± 8.1
Postop 10–20 min	43.7 ± 6.2	36.6 ± 5.6	43.2 ± 5.6
Postop 30–40 min	47.2 ± 6.6	37.6 ± 5.9	44.3 ± 6.3
Postop 50–60 min	53.0 ± 6.5	41.6 ± 5.5	43.2 ± 6.1

Mean ± SEM

**P* < 0.05 vs LS.†*P* < 0.05 vs LS.*P* < 0.005 vs C.*P* < 0.005 vs C.*P* < 0.005 vs baseline.*P* < 0.05 vs baseline.

S (ten per cent) groups during an hour stay in the recovery room. The morphine dosage ranged from 2–4 mg IV and was not correlated to the occurrence of apnoea among the patients.

Discussion

Our data show that sufentanil reduced the thiopentone requirement for induction of anaesthesia in the LS or S groups by 28 and 40 per cent respectively in unpremedicated young healthy individuals (Table I). The most marked responses in heart rate (HR), systolic (SBP) and diastolic blood pressures (DBP) were manifested at one minute after tracheal intubation in the control group. The supplementation of lidocaine, which has been shown to suppress the cough reflex²⁰ and to blunt hypertension and tachycardia during tracheal intubation,²¹ with low-dose sufentanil was as effective as sufentanil alone in a conventional dose in blunting the cardiovascular responses to intubation (Figures 1–3) in our study. One patient in each of the LS and S groups exhibited bradycardia following tracheal intubation when anaesthesia was maintained with 33 per cent O₂-N₂O without surgical stimulation. Blood pressures were stable and the heart rates increased promptly following atropine IV 0.6 mg. No hypotension or rigidity was observed in any subject.

The major objective of this study was to compare the two treatment groups with respect to postoperative respiratory depression in outpatient surgical procedures. Although cases of respiratory depression after sufentanil have been reported,^{7–11} this depressive effect has only been estimated grossly by a decrease in respiratory rate or by cyanosis in patients after operation. It is the clinical impression that patients need to be stimulated constantly in the recovery room after sufentanil anaesthesia. In the present study, the respiratory induction plethysmography (RIP)^{16–19} was used to measure postoperative respiratory functions in the recovery room. This allowed continuous monitoring of ventilation with minimal disturbance to patients, making it ideal for assessing postoperative respiratory function in the “natural” recovery room setting. However, it did not measure the patient's ability to respond to hypercarbia or hypoxaemia.

The effect of isoflurane on postoperative respiratory function was minimal in our study groups. The isoflurane vaporizer was turned off at least five to eight minutes before the termination of surgery. As well, the maximum isoflurane inspiratory concentration was never higher than 0.5 per cent in the sufentanil groups, being typically about 0.25 per cent for the LS group and minimally on and off for the S group. Although halothane and enflurane have been shown to reduce the hypoxic reflex proportionally more than ventilation and the carbon dioxide response, even at 0.1 MAC sedation dose in humans,²² all our patients had zero end-tidal isoflurane concentration prior to tracheal extubation in the operating room. Also, arterial oxygen saturation was 99 per cent in all patients during the recovery period.

The circulatory changes seen during tracheal intubation

have been ascribed to reflex stimulation of the autonomic nervous system.²³ Many methods have been used to attenuate the adverse response to laryngoscopy and intubation including increasing the depth of inhalational anaesthesia,²⁴ narcotic analgesics,³⁻⁵ lidocaine,¹⁵ vasodilators²⁵ and beta blockers.²⁶ Lidocaine IV has been found to suppress the cough reflex,²⁰ to prevent increases in intracranial pressure,²⁹ to attenuate circulatory responses²¹ and to possess anti-arrhythmic properties.²⁸ In the present study, we utilized these effects of lidocaine in supplementing low-dose sufentanil to achieve a balance in haemodynamic control and postoperative respiratory depression than just from the conventional dose of sufentanil.

The dose of lidocaine used in the LS group at induction of anaesthesia would have had no effect on postoperative respiratory function after 70 min of surgery. Pharmacokinetically, the plasma concentration of lidocaine is very low 70 min after IV injection. A blood level of $3 \mu\text{g} \cdot \text{kg}^{-1}$ is reached between 2–5 min after IV lidocaine administration.²⁹ About 70 per cent lidocaine is bound to plasma proteins, distribution is rapid and its apparent volume of distribution is about $1 \text{ L} \cdot \text{kg}^{-1}$.³⁰ Pharmacodynamically, subtle neurological symptoms may occur only at plasma concentrations near $5 \mu\text{g} \cdot \text{kg}^{-1}$. Therefore, we believe that the postoperative respiratory function measured by the RIP reflect the effects of sufentanil used in the study groups.

Low doses of sufentanil have been reported to produce both longer³¹ and shorter³² durations of respiratory depression than equivalent doses of fentanyl, but rigorous, quantitative measurements of respiratory drive were not employed in those studies. Brizgys *et al.*³³ compared sufentanil 0.5 and $1.0 \mu\text{g} \cdot \text{kg}^{-1}$ as an adjunct to thiopentone induction of anaesthesia. They found all patients' tracheas could be extubated at the end of the operation without the need for narcotic antagonists. However, their surgical duration ranged from 25 min to 8.5 hr. In the present study, although postoperative arterial oxygen saturation was well maintained at 99 per cent with supplemented oxygen, PaCO_2 was significantly elevated in the S group 30 minutes postoperation (Table II). Postoperative ventilatory patterns were significantly different among the three groups. The control group showed the most regular respiratory pattern; recurrent apnoea and compensatory hyperventilation were common in both active treatment groups but were most marked in the S group. Our data showed that the initial 10–20 min after operation was the most vulnerable period for patients to develop postoperative respiratory depression. The mean apnoea index was higher ($P < 0.005$) in the S group especially in the initial 10–20 min period after operation (Figure 4). The mean apnoea index tended to decrease

over an hour of observation whereas no decrease was observed in S group. The mean apnoea duration, among those patients with apnoea, showed a dose relationship of 10.3, 12.6 and 16.5 sec in groups C, LS and S respectively, in the initial 10–20 min after operation (Figure 5). This suggests the importance of close observation in these patients in the initial 10–20 min after surgery. No difference was found between the LS and control groups in both apnoea index and apnoea duration. Although there is a 0.3 chance of a type-II error for the LS group to be different from control in the apnoea index measurement (Figure 4), the likelihood of a type-II error in the apnoea duration is 0.002 between the two groups (Figure 5) over the initial 10–20 min period after operation.

Detailed postoperative pulmonary function (Table III) also indicated that the most vulnerable period was at the initial 10–20 min and that patients in the S group showed significantly decreased respiratory rates and prolonged expiratory times. However, RIP does not measure the hypercarbic or hypoxaemic responses in patients. Greater analgesia in the recovery period for the S and LS groups was also suggested in the number of patients requiring supplemental postoperative analgesia.

In summary, our findings indicate that, when the conventional induction dose of sufentanil ($1 \mu\text{g} \cdot \text{kg}^{-1}$) is used in balanced anaesthesia for surgical procedures less than 70 min, considerable risk of postoperative respiratory depression overrides its advantages in attenuating the pressor responses to intubation. The use of low-dose sufentanil ($0.5 \mu\text{g} \cdot \text{kg}^{-1}$) with lidocaine ($1.5 \text{ mg} \cdot \text{kg}^{-1}$) achieves comparable attenuation of pressor responses to intubation and with minimal respiratory depression.

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