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Automatic CPAP Compared with Conventional Treatment for Episodic Hypoxemia and Sleep Disturbance after Major Abdominal Surgery

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Background: **After major surgery, analgesia with opioids can cause obstructive apnea and intermittent hypoxemia, probably from loss of upper airway control. Since this resembles the obstructive sleep apnea syndrome, we tested the possibility that nasal continuous positive airway pressure (nCPAP) would reduce episodes of reduced oxygen saturation and sleep disruption. Because oxygen therapy is frequent after surgery, we also assessed the effect of oxygen on sleep disruption.**

Methods: **We recruited 48 patients about to have major abdominal surgery. We present data for 34 patients: 27 who received patient-controlled intravenous morphine and 7 who received epidural opioid. Treatment was randomized to either nCPAP or conventional therapy with an oxygen mask. Alternate periods of administration of air and 35% oxygen were used in both groups. If the oxygen saturation as measured by pulse oximetry was consistently <90% on air, the patient was withdrawn from the study. We measured sleep, arousals, oxygenation, episodes of desaturation, and disturbances of respiration. Values are given as median and quartiles.**

Results: **The median proportion of time awake was 65% (45–79%) among control patients and 74% (55–87%) among those undergoing nCPAP. Oxygen administration did not affect the sleep pattern. The median frequency of arousals per hour of sleep was very similar in each group: during air breathing from nCPAP, 125 (76–187), and during air breathing by mask, 116 (84–187). Oxygen therapy had no effect. Oxygenation and hypoxemic events were not improved by nCPAP. Oxygen therapy improved oxygenation and reduced but did not eliminate episodes of desaturation.**

Conclusions: **Nasal CPAP does not improve sleep and oxygenation or reduce hypoxemic events in the first night after major abdominal surgery.**

This article is featured in "This Month in Anesthesiology." Please see this issue of ANESTHESIOLOGY, page 5A.

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AFTER major abdominal surgery, patients have repeated episodes of upper airway obstruction, hypoxemia, and sleep disruption.[1,2] These episodes have been associated with heart rate and ischemic electrocardiographic changes.[3–5] Although oxygen therapy reduces the incidence and severity of hypoxemia,[6–9] oxygen therapy probably does not affect the incidence or severity of episodes of obstruction.[8,10]

Episodes of obstruction in the postoperative patient resemble the episodes seen in the sleep apnea–hypopnea syndrome (SAHS). SAHS can be effectively treated with nasal continuous positive airway pressure (nCPAP), which reduces obstructive episodes, reduces the incidence and severity of hypoxemic episodes during sleep, and relieves daytime drowsiness.[11] In patients with SAHS, obstructive episodes disturb sleep, activate the sympathetic system, and may cause hypertension. These effects are reduced by nCPAP.[12]

We considered the possibility that if nCPAP could prevent episodic airway obstruction, it would reduce hypoxemia and improve sleep for patients after surgery.

Although oxygen therapy is widely recommended for the prevention of postoperative hypoxemia, it may not be entirely without adverse effects. If an episode of obstruction causes less hypoxemia when oxygen is given, the stimulus to arousal will be less, and the duration of obstruction can become longer.[13] A possible advantage of oxygen treatment is that prevention of hypoxemia could limit hyperventilation and consequent hypocapnia after relief of the obstruction and hence reduce the tendency to cyclical episodes of obstruction.[14] Therefore, we also tested the possibility that oxygen therapy might alter the frequency of sleep disturbance.[15]

Materials and Methods

The study was approved by the local research ethics committee, and patients gave written consent. We recruited patients who were about to have elective major abdominal surgery and who would be cared for in a high-dependency unit for at least one night after surgery. None of the subjects had symptoms of sleep-disordered breathing, such as excessive sleepiness, or poor daytime function.

Patients were shown the monitoring system on the day before their surgery and were fitted for the nasal mask (at this time, the allocation of the patient to active or

conventional treatment had not been made). All patients spent the night before their surgery in a normal surgical ward, and many underwent bowel preparation causing diarrhea, which often caused disruption of sleep.

Patients were visited on the evening after surgery to ensure that they still wished to participate. We randomly allocated patients, using a sealed-envelope system, to receive either nCPAP or conventional therapy with an oxygen mask. We recognized several factors that might affect the incidence of hypoxemia and sleep disturbance and stratified the randomization to take them into account.

Separate randomization was done for the mode of analgesia (patient-controlled intravenous morphine [PCA] *versus* continuous epidural infusion) and for sex, age ($<$50 or $\geq$50 yr), and weight (less than expected body weight or greater than or equal to expected body weight, with body weight predicted on the basis of sex, age, and height). Finally, the random allocations to nCPAP or Venturi oxygen mask were blocked in random groups of 6. Four allocations were drawn from each block. The two supplementary allocations were available in case a patient withdrew from the study after treatment allocation, to prevent the operator from being able to predict the allocation in the last case of each block.

We used a portable polysomnographic monitoring system (P-series 2; Compumedics, Victoria, Australia) with a 20-MB flash card.

The electroencephalogram (EEG) was recorded from scalp positions Cz–Pz and F3–F4, along with the electrooculogram and submental electromyogram. Thoracic and abdominal respiratory movements were measured with strain-gauge bands. A finger probe was taped to a finger to provide a pulse oximeter signal, and a precordial electrocardiographic signal was recorded. In the subjects breathing from the Venturi oxygen mask, oronasal airflow was recorded with thermocouples.

The technical quality of the signals was checked by displaying the signals and ensuring that the electrode impedances were $<$5 kOhm. The electrode and sensor cables were connected to a small patient interface box and then by a single cable to the bedside data recorder. Studies started at about 23:00, and we analyzed the first 6 h of recording so that we could obtain equal periods of oxygen and air treatment.

Data stored in the portable system were transferred later to a reader station (Compumedics S series) and analyzed for sleep stage by an experienced operator. Each record was divided into 30-s epochs. Sleep was scored from Cz to Pz with use of standard scoring criteria.[16]

Preliminary data for postoperative patients showed that in the wakeful state, associated with persistent submental electromyographic activity, when α EEG activity would be expected, the EEG could have unusually slow frequencies. These would normally be θ frequencies (4–7 Hz). We concluded that this was an effect of the morphine,[17,18] and for this study we modified the standard criteria and used a frequency of 4 Hz to distinguish wakefulness from stage 1 sleep.

We measured the sleep records for time awake and time in each stage of sleep and expressed this as a percentage of the time available for sleep. An arousal was defined as a return to α or θ activity on the EEG for at least 1.5 s, with a concurrent increase in submental electromyographic activity, however brief.[19] Arousal frequency was calculated as the number of arousals per hour of sleep for each subject in each treatment period. An episode of oxygen desaturation was noted as any reduction of the oxygen saturation reading of $\geq$2%, in comparison to the immediately preceding value, and the magnitude, frequency, and duration of these events were recorded automatically by the Compumedics software.

We assessed the incidence of apneas–hypopneas during sleep with use of standard definitions for our laboratory. Apnea was defined as the absence or almost complete cessation of airflow signal for $>$10 s. Hypopnea was a decrease in rib cage or abdominal movement to $<$50% of a preceding baseline signal for more than 10 s. The incidence was measured as the absolute number in each 30-s epoch and also was calculated as the number per hour of sleep for each subject in each treatment period.

Nasal CPAP was applied with use of the Autoset (version 3.03; ResMed UK, Oxford, United Kingdom). This device automatically applies positive pressure to the nasal mask in response to abnormalities of the breathing pattern. Pressure increments are applied in relation to apnea, snore, flattening index,[20] existing pressure, and leak. It commences with a pressure of 4 cm H_2O and adjusts the applied pressure according to the time course and magnitude of the inspiratory flow. The pressure applied, breathing pattern, and degree of mask leak were recorded and subsequently analyzed. The flow signal allows an index of frequency of apneas and hypopneas, related to the time that the system is switched on. Unfortunately, this yielded an indication of respiratory disturbance that differed from the index obtained for the control patients, in which disturbances were related to the amount of time that the patient was asleep.

Abnormalities of inspiratory flow were quantified with the flattening index.[20] This index is an indication of the limitation of flow during inspiration, caused by dynamic collapse of the upper airways, which flattens the normally rounded inspiratory flow waveform. A normal index is 0.3, and a smaller value indicates inspiratory flow limitation. Severe flattening yields an index of $<$0.05, and trivial flattening yields values between 0.10 and 0.15. However, if the Autoset functions correctly, the applied pressure will increase to improve the flow pattern, flattening will be prevented, and the index should

be maximized. For all patients, the nasal mask was fitted and the apparatus set up by a single trained and experienced technician, who was accustomed to fitting masks to patients with SAHS. The same technician set up and supervised the patient sensors and recording system.

Previous devices used for administering oxygen *via* nCPAP devices could deliver variable inspired concentrations.[21] To give a known concentration, we made and fitted a wide-bore manifold, supplied by a 35% Venturi oxygen device, to the air inlet of the Autoset. The manifold discharged into a wide-bore reservoir tube. In this way, the Autoset "inspired" from the gas mixture provided by the Venturi and had a large low-resistance reservoir if the inspired flow transiently exceeded the delivery rate of the Venturi system. Testing this device showed that the delivered concentrations were stable and always within 2% of 35%.

Gas was supplied to the 35% oxygen Venturi from an electrically operated solenoid valve controlled by a programmable time switch. The valve provided either oxygen or air from cylinders, *via* flow adjusters. In this way, the patient could receive either oxygen or air from the nCPAP mask. The same switch was used to deliver oxygen or air to an oxygen mask of the Venturi type (Intersurgical, Wokingham, Berkshire, UK) if the patient had been allocated to conventional therapy. Oxygen and air were alternately supplied for 90-min periods, so that each patient would receive two periods of each in the night. We chose a duration of 90 min for each period of gas administration because this is the approximate cycle of normal sleep. A separate pulse oximeter probe attached to the ward monitor showed a reading for nursing use: if this reading was consistently $<90\%$, the timing device was inactivated, oxygen was supplied continuously, and the patient data were not used, because comparisons with air breathing could not be made.

Before the sleep records were scored they were divided into segments according to the inspired gas, made anonymous, and then replayed in random order, without the oximeter trace, so that the operator scoring the record was unaware of the patient identity or treatment. For each patient, we analyzed two 90-min periods on air and two on 35% oxygen, starting at the onset of the recording period.

Anesthesia was standardized and consisted of administration of an oral benzodiazepine (temazepam) for premedication, induction of anesthesia with propofol, maintenance of anesthesia with isoflurane and nitrous oxide, muscle relaxation with either atracurium or vecuronium, and administration of morphine for intraoperative analgesic supplementation. After surgery, patients were nursed in a high-dependency unit that has eight beds in a single large area. The nurse:patient ratio is at least 1:2, and the unit is almost always fully occupied. Pain was scored hourly by the patient, on the basis of a 4-point scale for pain at rest and on movement. The scale rates no pain as 0, mild pain as 1, moderate pain as 2, and severe pain as 3. The pain score was S for sleeping patients, who were not woken. Analgesia was considered satisfactory if the score was S, 0, or 1 at rest and up to 2 on movement.[22]

Statistical Analysis

In a previous study of patients of this type, airway obstruction occurred in 90% of subjects and was present up to 70% of the time, and hypoxemia was frequent when oxygen was not given.[10] If the effects of nCPAP were the same as in the treatment of SAHS, the therapy would reduce the incidence of obstructive episodes by 90%. However, we recognized that the subjects would be relatively heterogenous in age, sex, obesity, surgery, and coincident respiratory disease and that such factors would reduce the power of the study. Analysis by intention to treat would also reduce the power because some patients might not tolerate the treatment and would be withdrawn. We estimated that a sample size of 30 would provide a power of >0.9 to demonstrate an 80% difference in arousal episodes.

We tested *a priori* that nCPAP would improve sleep (reduce the incidence of arousals, increase sleep duration, and improve the quality of sleep) and oxygenation (reduce the frequency of episodes of desaturation in patients breathing air or oxygen and improve oxygenation in patients breathing air). We tested for differences in these variables between the groups with use of the Mann–Whitney *U* test for unpaired data.[23] Because we made these predictions before the study, we made no correction for multiple comparisons. We also planned *a priori* to compare the effects of air or oxygen, within subjects, on the same variables, by using the Wilcoxon test. During the analysis of the results we made a further comparison with the Wilcoxon test for paired data, contrasting episodes of desaturation in the same subjects awake and asleep.

We used custom-written software for preliminary data processing from the Compumedics and ResMed systems, Excel 97 (Microsoft, Redmond, WA) for data-handling and SPSS version 7 (Chicago, IL) for statistical analysis. Incidental comparisons of other data were with the chi-square test or tests for categorical trends. Patient data are generally presented as median and interquartile values because the values showed considerable range and were not necessarily normally distributed.

Results

We recruited 48 patients. Of these, seven were eliminated before randomization. One patient unexpectedly underwent a laparoscopic procedure only, one was too unwell after the operation, and five declined application of the monitoring apparatus, before randomization. One

Table 1. Distribution of Treatment, Analgesia, and Physical Characteristics of the Patients Studied

Type of Analgesia			Males		Females	
			Underweight	Overweight	Underweight	Overweight
Patient-controlled analgesia (n = 27)	nCPAP	Number	7	2	4	1
	(n = 14)	Mean age (yr)	65	58	57	59
	Control	Number	8	0	4	1
	(n = 13)	Mean age (yr)	62	—	63	53
Epidural analgesia (n = 7)	nCPAP	Number	2	0	1	0
	(n = 3)	Mean age (yr)	76	—	41	—
	Control	Number	3	0	1	0
	(n = 4)	Mean age (yr)	53	—	64	—

nCPAP = nasal continuous positive airway pressure.

patient was randomized to receive the nCPAP mask and then declined. We therefore enrolled 40 patients in the study.

There were no obvious systematic differences between the patients allocated to nCPAP and those who received control treatment. The female patients included two younger subjects, aged 28 and 36 yr, who were undergoing surgery for colitis. Most of the patients were undergoing surgery for gastric, biliary, pancreatic or colon cancer, and there were no clear differences between the physical characteristics and modes of analgesia used for the different groups. Epidural analgesia was used for 8 of the 40 patients, and there was a slight preponderance of males (6 patients) in comparison with the overall number of males (25) in the study. Analgesia was rated as satisfactory in all the patients. Morphine consumption in the subjects receiving PCA was comparable between the groups (nCPAP, 31 mg, 12–54; control, 28 mg, 10–48). PCA morphine was provided for supplementary analgesia in the patients receiving thoracic epidural infusions, and there were no obvious differences in morphine consumption in those patients.

For two subjects (one treated with nCPAP), data were not recorded successfully. In four subjects (three nCPAP, one control), oxygen saturation while they breathed air was consistently <90%, and these patients were given 35% oxygen for the remainder of the study. Three of these excluded patients were >20% overweight. The number of subjects in the final comparisons was therefore reduced to 34, and the characteristics of these patients are given in table 1.

Application of the nCPAP mask was achieved satisfactorily for all the subjects assigned to receive this treatment. Obtaining a mask seal was difficult in patients with nasogastric tubes, and extra sealing materials were needed. Two patients had a gas leak from the mouth, but a chin strap was fitted to close the mouth, and this allowed satisfactory pressure levels to be obtained.

Once correctly set up, the Autoset provided low airway pressures, indicating that airway collapse, if present, could be easily overcome. The characteristics of the nCPAP settings are shown in table 2. The airway pressures were consistently small, and the values for the flow waveform and leaks were acceptable. There were no significant differences when the air and oxygen periods were compared (table 2).

The general pattern of sleep was very poor. Overall, the patients slept for 34% of the time. Six patients achieved stage 3 sleep, and there was no detectable stage 4 or REM sleep. One patient (male, control therapy, PCA) achieved stage 3 sleep for 46 min within 100 total min of sleep. Including the sleep of this patient, only 3.6% of sleep in the entire study was stage 3, and the frequency of stage 3 sleep is not analyzed further. The sleep patterns of the patient groups are summarized in table 3.

There was no difference in the pattern of sleep associated with nCPAP *versus* control therapy. The inspired oxygen fraction did not significantly affect the pattern of sleep (paired comparison). Inspection of the data suggested that control patients might be spending more time in stage 2 sleep (20; 5–39%) than those receiving nCPAP (11; 1–32%), but this was not confirmed statistically. The range of times spent in stage 2 sleep by different patients was great: the interquartile values for the mean proportion of time in stage 2 sleep lay between 1 and 40%.

Arousal from sleep was frequent and often was for short periods, without transition to wakefulness, and not related to changes in breathing pattern (fig. 1) Table 3 shows the patterns of sleep disturbance, as indicated by arousal frequency. There was no clear difference between the nCPAP and the control therapy groups. Inspired gas composition did not affect disturbances: the

Table 2. Comparison of Respiratory Measures during Oxygen and Air Breathing *via* the Autoset nCPAP System

	Air	Oxygen
CPAP pressure > zero (cm H_2O)	5.5	5.6
	4.6–6.1	4.5–6.4
Flattening index	0.20	0.19
	0.18–0.22	0.17–0.22
Proportion of mask leaks more than 0.4 l/min	0	9
	0–17.5	0–29

Values are medians and interquartiles.

nCPAP = nasal continuous positive airway pressure.

Table 3. Sleep Architecture and Sleep Arousals in the Study Groups

Treatment Group	Inspired Gas	% Wake	% Stage 1: Sleep	% Stage 2: Sleep	Arousals/h
nCPAP	Air	77 (44–87)	12 (4–16)	11 (1–30)	142 (93–200)
	35% oxygen	71 (58–87)	10 (7–15)	11 (2–33)	112 (75–168)
Control	Air	63 (46–79)	14 (5–17)	21 (11–39)	113 (82–169)
	35% oxygen	67 (41–78)	12 (4–17)	18 (3–38)	120 (91–192)

Values are median and interquartile values.

nCPAP = nasal continuous positive airway pressure.

mean difference in disturbances was 1 (−30 to +23) arousal/hour, in a comparison of oxygen- and air-breathing periods.

Respiratory disturbances were much less frequent than sleep disturbances. The incidence of apnea–hypopnea is shown in table 4. The data are not directly comparable for the control and treatment groups. Events in the control group were measured during sleep. Events in the nCPAP group were measured throughout the time that nCPAP was applied and had to be classified without the nasal thermistor signal. There was no relation between the incidence of respiratory events and the incidence of arousals in individual control subjects. Some respiratory disturbances ended with arousal, as shown in fig. 2. However, arousals were frequent in the absence of respiratory disturbance.

The use of nCPAP did not affect the pattern of oxygenation (fig. 3). During air-breathing, the proportion of time for which the oxygen saturation, as measured by pulse oximetry, was between 91 and 95% was 69% (45–90%) for the patients undergoing nCPAP and 62% (17–87%) for the control patients. Giving 35% oxygen improved arterial oxygenation and resulted in saturation values >95% for 92% (47–95%) of the time in the patients undergoing nCPAP and 84% (59–91%) of the time in the control patients. The improvement in oxygenation was not significantly different in the two treatment groups.

Episodes of desaturation were similar in the nCPAP and control therapy groups (fig. 4). However, increased inspired oxygen reduced the incidence of desaturation by about 50% ($P < 0.01$).

Our original hypothesis was that nCPAP would prevent episodes of obstructive apnea that occurred during sleep. The patients in this study slept badly. We therefore considered the possibility that nCPAP might have a useful effect during sleep only. Consequently, we reanalyzed our data to compare the effects of treatment with nCPAP and inspired oxygen in relation to the sleep state, although this had not been our initial intention. The beneficial effects of oxygen were still evident, and treatment with nCPAP had no effect either during sleep or in the awake state (fig. 5).

In addition, the frequency of desaturation was greater when patients were classified as awake ($P < 0.01$; Mann–Whitney test for ordered variables).

Discussion

This study was technically difficult. Patients who have had major surgery are often reluctant to undergo unnecessary interference, even if their pain is well treated. Sensor adhesion was often poor because of sweating, and access was hampered by equipment such as nasogastric tubes, intravenous infusions, drains, catheters, dressings, and the routine ward monitors. Nausea, vomiting, and pruritus impeded continuous monitoring.

In the current study, satisfactory electromyographic recordings were difficult to obtain, and reapplication of

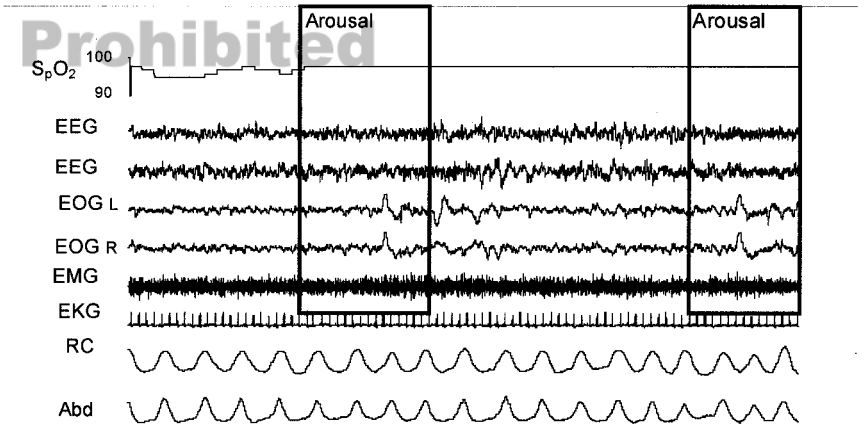

Fig. 1. A representative trace showing arousals from stage 2 sleep. The horizontal time marks are 10 s, and the trace shows two successive epochs. Both are classified as sleep because >50% of the time in each is a sleep pattern. Note that the respiratory movements show no disturbance. The short initial decrease in the oxygen saturation ([S]po_2), as measured by pulse oximetry, is probably an artifact, because there was no preceding respiratory change. EEG = electroencephalography; EOG = electro-oculography; EMG = electromyography; EKG = electrocardiography; RC = rib cage; Abd = abdomen.

Table 4. Incidence of Apnea/Hypopnea

	Air		Oxygen	
	nCPAP	Control	nCPAP	Control
Total Apnea/Hypopneas	12 (1–41)	8 (1–23)	14 (4–87)	12 (4–38)
Apnea/Hypopneas/h	4 (1–14)	8 (0–26)	5 (1–20)	9 (6–36)

Values are median and interquartile values; The index for patients receiving nCPAP is for hours in bed, and the index for control patients is for hours slept.
nCPAP = nasal continuous positive airway pressure.

one or more of the sensor systems was needed in 15 patients. In one case, complete failure of recording necessitated withdrawal of the patient from data analysis. Although we had assessed each patient before surgery, mask-fitting without leaks was awkward. Once it was fitted, however, the pressure monitor provided a good measure of adequate therapy, and patients tolerated the treatment well.

We chose the P series Compumedics apparatus because it has been used successfully in other large studies. In a study involving 6,697 participants, 87% of recordings, made without continuous supervision, were of good quality or better.[24] We have reported on the use of the same measurement system in more than 150 patients.[25]

Chest wall movement in patients after major surgery can be abnormal, particularly in the presence of airway obstruction.[10] The data we obtained could not be scored in identical ways because we did not have a synchronous nasal signal in the subjects treated with nCPAP, and the flow signals had to be measured with different devices. Polysomnographic scoring of respiratory disturbance depends on the reduction or absence of nasal flow with

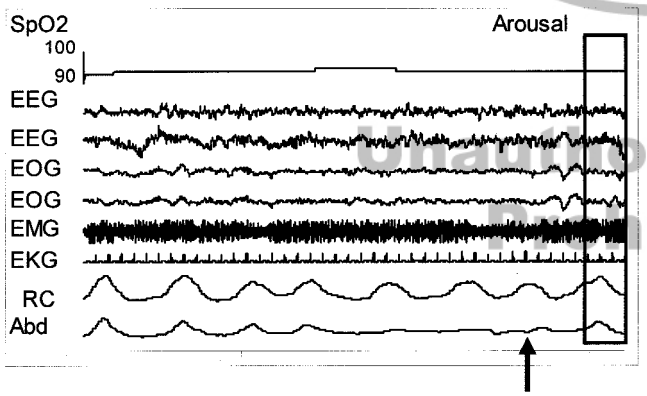

Fig. 2. An example of a trace showing a typical obstructive hypopneic episode, in the same patient as for fig. 1. Time marks are 10 sec. The patient is in sleep stage 1. At the start of the sample, oxygen saturation (Spo_2) is recovering from a previous obstructive episode without arousal. Abdominal (Abd) excursion is progressively reduced, to a greater extent than rib cage (RC) expansion. Finally, there is paradoxical inward movement of the abdomen as the rib cage moves out (arrow), followed by a large normal breath and arousal from sleep, indicated by the boxed area. EEG = electroencephalography; EOG = electrooculography; EMG = electromyography; EKG = electrocardiography.

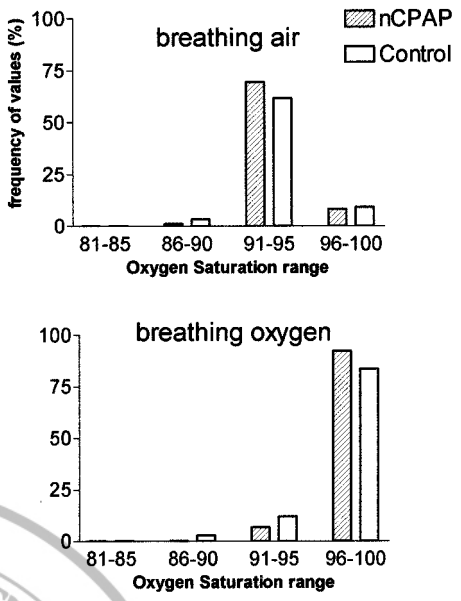

Fig. 3. Pulse oximeter saturation (Spo_2) values in the patients randomized to nasal continuous positive airway pressure (nCPAP; hatched columns) and control treatment (open columns) while breathing air (upper panel) and 35% oxygen (lower panel). There was no significant difference in the distribution of times spent at the different saturation values, in relation to treatment group (Mann–Whitney test for ordered categories).

paradoxical chest wall movement, with the rib cage being drawn in during inspiration. This is not characteristic of the events during airway obstruction in the postoperative patient.[10]

In the current study we also noted that hypopneas resembled those we have previously reported as occurring in patients after surgery and were not like those observed in patients with sleep apnea; we must be cautious in the recognition of respiratory disturbances. However, there is no doubt that the respiratory disturbances we detected were much less frequent than the arousals, and an alternative reason for arousals should be sought.

Because the study premise was that respiratory obstructive events were indeed responsible for disturbances of sleep, we did not plan to assess other potential causes. However, the patients were in a large room with other patients, the environment was not quiet, and disturbances of many types were likely frequent and could have caused at least some of the arousals.

Some of the conventions used in reporting on sleep polysomnography, which we have used carefully and consistently, could cause confusion in interpretations of our results. In particular, an arousal is defined as a transient return to the awake state from sleep and does not necessarily lead to a longer period of wakefulness.[19] An epoch of measurement 30 s in duration will be classified as a period of wakefulness if it includes <15 s of sleep. However, this epoch can also contain an arousal, if it occurs in the remaining short period of sleep in the

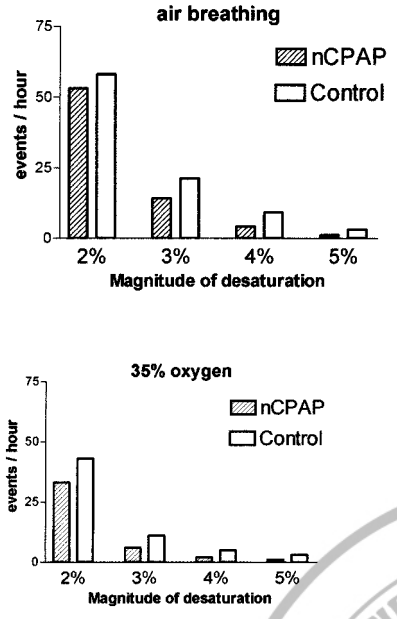

Fig. 4. Effects of oxygen and nasal continuous positive airway pressure (nCPAP) on episodes of desaturation. The frequency (episodes per hour) of decreases in baseline oxygen saturation of 2–5%, is shown in relation to treatment (nCPAP = hatched columns; control = open columns) and in relation to inspired oxygen concentration (upper panel = breathing air; lower panel = breathing 35% oxygen).

epoch. The arousal will appear to have occurred during an epoch classified as "wake."

The arousal rate is expressed as arousals per hour of sleep. This rate will be great if the patient is having frequent short periods of sleep that allow arousals to be noted but that are too short to allow the periods to be classified as sleep. We have no data from the current study to indicate the proximity of arousals to awakenings.

After major abdominal surgery, lung function is impaired and hypoxemia persists for several days. Attempts to improve lung function and reduce complications by improved analgesia have been generally disappointing.[26–28] In addition to a persistent defect in oxygenation, postoperative patients have repeated episodes of hypoxemia, most likely associated with upper-airway obstruction.

Most middle-aged people have occasional apnea during sleep,[29] and such episodes become more frequent and longer after use of sedatives and analgesics.[30] Episodic hypoxemia occurs in almost all patients given opioid analgesics after major abdominal surgery,[1] and these are no less frequent when different routes of administration are used, such as continuous thoracic epidural analgesia or patient-controlled analgesia.[31]

However, the exclusive use of pulse oximeter recordings may overestimate postoperative hypoxemic events, as some may be artifacts.[32] In our study we applied the probe firmly with adhesive, but some episodes could have been artifacts. Oxygen therapy reduced the incidence of mild and moderate episodes of desaturation considerably, and this is a biologically plausible effect. The same effect might have been expected in the severe, infrequent decreases of >5%, but this was not apparent.

This easily detected effect of oxygen suggests that artifacts are uncommon and may cause infrequent severe events (or perhaps infrequent events of all magnitudes) (fig. 4). This finding also suggests that the spectrum of mild and moderate hypoxemic events, which are more frequent, may provide a better index of respiratory disturbance than analysis of more severe events, which are infrequent and may contain a greater proportion of artifacts.

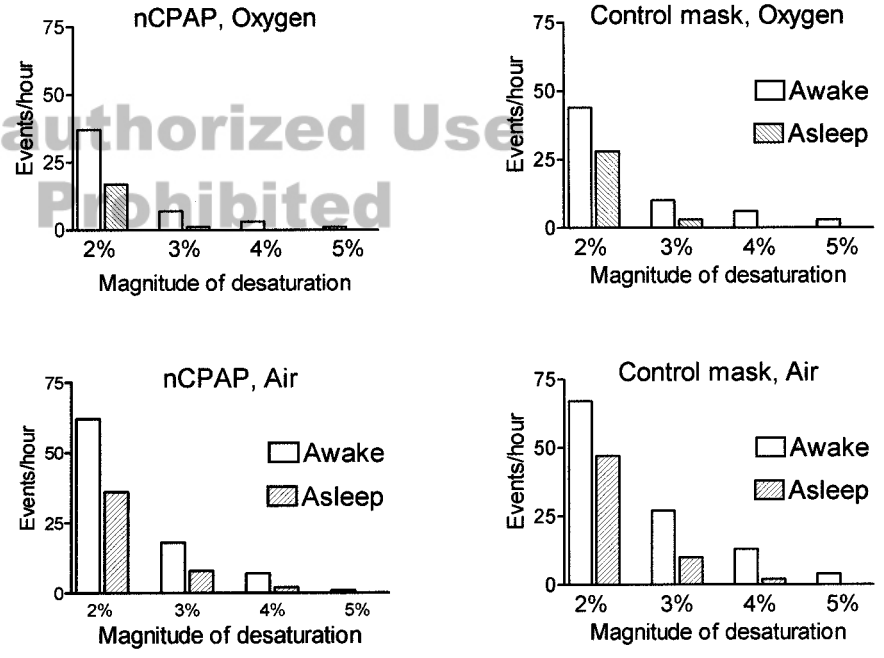

Fig. 5. Influence of treatment and sleep state on episodes of hypoxemia (open columns = awake; hatched columns = asleep; upper panels = breathing 35% oxygen; lower panels = breathing air). Desaturation events were significantly more frequent in the awake subjects ($P < 0.01$).

The prevalence of hypoxemia in the night before surgery has been related to abnormalities in the pharynx, but after surgery, abnormalities of lung function assume greater importance.[33] Features of patients before surgery, such as a history of sleep-disordered breathing or poor oxygenation during sleep, can predict postoperative hypoxemia and episodes of desaturation.[34]

Oxygen therapy is usually successful in preventing both continuous and episodic hypoxemia and can reduce tachycardia, particularly in the more hypoxemic patient.[35] However, oxygen therapy is rarely continued for more than the second postoperative night, and the apparent incidence of hypoxemia may be greater in subsequent nights.[7] Although oxygen may prevent hypoxemia, the cyclical episodes of airway obstruction continue and have been associated, in a single study, with abnormal chest wall mechanics.[10] In fact, oxygen therapy may increase the duration of obstructive episodes in patients with SAHS.[15]

Cycles of airway obstruction and arousal in patients after surgery may be harmful: they are associated with cardiovascular effects such as tachycardia, hypertension, and ischemic electrocardiographic changes.[3,5,36] Oxygen therapy is not generally successful in abolishing these cardiovascular events. In addition, repeated arousals from sleep cause sleep fragmentation and alter the structure of sleep, with less deep and REM sleep, and later "REM rebound."[37]

Sleep deprivation can impair ventilatory responses to hypoxia and hypercapnia[38] and can increase the likelihood of airway obstruction.[39] Loss of sleep can impair cognitive function and can cause confusion in the elderly.[40] Delirium and confusion are recognized as risk factors for atelectasis, pneumonia, and death due to respiratory complications.

Sleep disturbance is common after surgery[41–44] and appears to be more related to the surgery or perhaps the postoperative analgesics than to the anesthesia. After laparoscopic cholecystectomy, even when no opioids were used for analgesia, the sleep pattern is altered, with less deep sleep and more stage 2 sleep.[45]

In patients with SAHS, oxygen therapy can prevent the hypoxemia that accompanies the obstructive episodes, but it is of no value in diminishing symptoms. In contrast, preventing the disruption of sleep pattern with CPAP improves mental function and quality of life.[46]

We tested this more fundamental approach to the treatment of episodic obstructive episodes after major surgery. Of those patients who remained in the study, only one was withdrawn because of inability to tolerate the treatment. The active treatment was well tolerated by the other patients allocated to nCPAP, and it is unlikely that poor compliance contributed to the result.

Arousal may be the result of increased respiratory effort rather than a specific stimulus.[47] The frequency of arousals is not well correlated with symptoms in SAHS,[25] but the conventional criteria for defining arousal appear to be too severe. Subtle evidence of arousal can be detected early in an apnea episode,[37] and body movements and variability in EEG depth seem to be better at predicting response to nCPAP than are full arousals.[48] The cardiovascular response to an apnea episode that does not terminate in a definite arousal[37] is as great as that after a full arousal. Hypoxemia correlates poorly with arousal in healthy persons,[49] and hypercapnia may perhaps be more important.[50]

Our most important finding was that nCPAP did not prevent impaired sleep, episodes of arousal, hypoxemia, and the episodes of desaturation that occur in patients after major abdominal surgery. Despite the parallels in clinical features, risk factors, and to some extent etiology between this condition and SAHS, treatment that is highly efficacious for SAHS has no effect after surgery. However, CPAP has been shown to prevent drug-induced airway obstruction in some circumstances, such as midazolam and opioid[51] or propofol anesthesia.[52]

We considered the possibility that the study did not have sufficient power to demonstrate a difference between the therapies. However, the incidences of arousals and episodes of hypoxemia were large and proportional and more than sufficient to reliably indicate an effect if one had been present. The influence of oxygen was clear and very highly significant (although these comparisons could be made within subject, which added to the power of these observations).

We found persistent mild episodes of moderate oxygen desaturation, despite oxygen therapy (table 3). To some extent, these observations support those of Rosenberg *et al.*,[8] who reported that oxygen therapy did not reduce episodes of decreased oxygen saturation. However, the events measured by Rosenberg *et al.*[8] were decreases of $\geq$5%.

Our results show that the proportion of such decreases is very small in comparison with decreases that are less severe (2–5%) and that oxygen therapy had no influence on their incidence. We did not detect any decreases to values of $<$80% and found a far greater incidence of mild episodes of hypoxemia. In addition, oxygen therapy was most effective in reducing the mild and moderate episodes of hypoxemia.

We were surprised to find episodic hypoxemia in awake subjects and particularly that it occurred more than in sleep. Few previous studies have measured both sleep state and oxygen saturation at the same time,[1,44] presumably because of the considerably greater technical difficulty than that of automatic logging of saturation values. In addition, the analysis of sleep records is technically demanding and time-consuming.

Catley *et al.*[1] measured sleep and stated that "pronounced oxygen desaturation and obstructive apneas *never* occurred while the patients were awake."[1] However, the time period that they used for categorizing

sleep is unclear, and they did not provide details of the amount of time that their subjects were sleeping.

Our finding that episodic desaturation was more frequent in awake patients could have resulted from our use of a standard definition for sleep. An epoch of 30 s is defined as sleep if >15 s of a characteristic pattern is noted in the epoch. If airway obstruction wakes a patient from a short sleep and this is followed by an associated transient decrease in oxygen saturation, then the patient could be classified as awake while a hypoxemic event occurred. In fact, there could be repeated short episodes of sleep with associated breathing disturbance and hypoxemia that are classified as mainly awake.

To substantiate this possibility, measurements of sleep state and arousals need to be made in relation to breathing pattern, by means of methods that are reliable postoperatively. We did not set out to do this, since the records for sleep and oxygenation were analyzed separately. Our recent studies support the observation that breathing disturbances are more frequent in the awake state.[53]

In summary, we found that nCPAP did not alter sleep, arousal frequency, or oxygenation after major surgery. Oxygen therapy did not affect sleep or arousals, but it reduced the frequency of mild episodes of desaturation. The frequency of desaturation was less when the subjects were classified as asleep. We conclude that hypoxemia after surgery is not strongly related to sleep pattern and that oxygen therapy is more effective than nCPAP in preventing hypoxemia.

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