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Depression of sighing in the first three postoperative days with epidural morphine analgesia

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Abstract: We have studied the effect of spontaneous sighs on maintaining arterial oxygenation in patients receiving epidural morphine for analgesia after upper abdominal surgery. Sixteen patients scheduled for elective gastrectomy were monitored continuously with pulse oximetry and respiratory inductive plethysmography (RIP) during one night preoperatively and for 60 h postoperatively with repeated arterial blood gas analysis. An average of 3.1 ± 1.2 (±SD) sighs were observed per hour preoperatively during sleep while postoperative sighs were significantly depressed to an average less than one per hour throughout the 60 h of the monitoring period ($P < 0.05$). Although postoperative Pao_2 values were significantly lower than preoperative values, there was no correlation between the decreases in Pao_2 values and number of sighs. Thus, it is unlikely that the long-term absence of spontaneous sighs observed may serve as a contributing factor for the long-lasting hypoxemia in the postoperative period.

Key words: Epidural morphine—Sighing—Postoperative hypoxemia

Introduction

Periodic spontaneous deep breaths or "sighs" are observed in humans from the neonatal period to adulthood. It has been suggested that sighs serve to maintain normal pulmonary functions by increasing lung compliance and thereby decreasing the work of breathing [1]. However, disagreement exists as to the effectiveness of sighs in improving pulmonary functions. Fletcher and Barber[2] demonstrated that in healthy young subjects spontaneous sighing was not followed by changes in lung mechanics or compliance and that almost complete absence of sighing for periods of 60–90 min following administration of intravenous morphine was not associated with changes in lung mechanics or intrapulmonary shunt.

Absence of sighs has been suggested as being one of the causative factors of the hypoxemia observed in the immediate postoperative period [3–5]. However, there has been no study showing the effectiveness of spontaneous sighs in maintaining arterial oxygenation during the later postoperative period, when atelectasis is more likely to occur. This study was designed to evaluate the frequency of spontaneous sighs and their roles in maintaining arterial oxygenation in the postoperative period in patients receiving epidural morphine for analgesia after upper abdominal surgery.

Materials and methods

After obtaining approval from the institutional ethics committee, 20 ASA class 1–2 patients scheduled for elective gastrectomy were studied. Exclusion criteria included advanced age (>65 years), any respiratory, cardiovascular or neuromuscular complications, and obesity.

Informed consent was obtained from each patient. All patients were monitored overnight prior to surgery with continuous pulse oximetry and respiratory inductive plethysmography (RIP) while asleep. Calibration of RIP was performed by the qualitative diagnostic calibration method [6].

The monitoring period was from 9:00 p.m. to 5:00 a.m., a duration of 8 h. The average number of sighs per hour during this period was calculated as the control.

On the day of operation, patients were premedicated with atropine sulfate 0.5 mg and hydroxyzine 50 mg i.m. 30 min prior to the induction of anesthesia. Upon arrival at the operating room, an epidural catheter was inserted into an interspace between T7 and T12. Anesthesia was induced with thiopental 4–5 $mg \cdot kg^{-1}$ i.v. followed by

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succinylcholine 1–1.5 mg·kg^{-1}, and the trachea of each patient was intubated with a cuffed endotracheal tube. Anesthesia was maintained with isoflurane (0–2%) in conjunction with N_2O (33%)/O_2. All patients received either pancuronium bromide or vecuronium bromide for muscle relaxation during surgery. No narcotics were given preoperatively or intraoperatively. On completion of surgery, muscle relaxation was reversed with neostigmine 2 mg and atropine 1 mg and the trachea of each patient was extubated in the operating room. Patients received 3 mg of morphine in 10 ml normal saline through the epidural catheter and were then transferred to the ICU. Thereafter, 10 of 20 patients received intermittent bolus injection of epidural morphine and the other ten received continuous infusion of epidural morphine with epidural patient controlled analgesia (PCA) for postoperative analgesia. Patients receiving bolus injection received morphine 2 mg in 10 ml normal saline epidurally twice a day (approximately at 8:00 a.m. and 8:00 p.m.) with supplementations of morphine 1 mg in 5 ml normal saline epidurally when pain was not endurable at rest. Those who received continuous and PCA epidural morphine were given explanation of the PCA system preoperatively. Their continuous epidural infusion of morphine was started on arrival at the ICU, and the rate was set at 0.2 mg/h, bolus injection at 0.3 mg with a lock-out interval of 45 min. We ensured that all patients were free of pain at rest.

RIP and pulse oximetry monitorings were replaced and continuous measurements were made from arrival at the ICU until the morning of the 3rd postoperative day. Arterial blood gas tensions and pH were determined preoperatively, on arrival at the ICU (0 h), and at 6, 12, 24, 36, 48, and 60 h thereafter. No supplemental oxygen was given throughout the monitoring period. Patients were withdrawn from the study if their Spo_2 values were continuously lower than 90% for more than 20 min or had they numerous apneas with episodic desaturations to values lower than 90%.

Respiratory rates and number of sighs were determined every 6th h from the records of RIP monitoring. A sigh was defined as a single spontaneous breath with at least twice the average tidal volume.

Data were analyzed with Student's *t*-test, Mann-Whitney U-test, and Wilcoxon's signed rank test. $P < 0.05$ was taken as the level of significance. Values were expressed as means ± SD.

Results

Of the 20 patients participating in the study, 4 were not able to complete the study because of numerous apneas and desaturations in the postoperative period. No patients were withdrawn from the study for having continuously low Spo_2 values for more than 20 min. Seven patients receiving bolus injection and nine patients receiving continuous and PCA epidural morphine were included in the analysis. No statistical differences were seen between the groups with respect to age, height, weight, preoperative pulmonary function testings, or total morphine dose (Table 1). Because intermittent bolus injection of epidural morphine and continuous with PCA epidural morphine produced qualitatively similar results as well as qualitatively similar analgesia, they will be considered together.

Figure 1 shows a representative breathing pattern during preoperative monitoring (Fig. 1A) and postoperative monitoring (Fig. 1B) observed in a single patient receiving continuous and PCA epidural morphine. During the preoperative monitoring period, three sighs were recorded in 20 min. However, in the postoperative period, the breathing pattern was regular with no spontaneous deep breath. These changes were similar in all the patients regardless of the analgesic regimens.

Postoperative Pao_2 values were all significantly lower than preoperative values, while postoperative $Paco_2$ values showed essentially no change from preoperative values except at 48 h (Fig. 2). Respiratory rates were significantly elevated during the 1st, 24th, 42nd, and 48th h postoperatively compared with the preoperative rates (Fig. 3).

The average number of sighs observed per hour during preoperative nights was 3.1 ± 1.2 (ranges 0–11). However, sighs in the postoperative period were significantly depressed to less than one throughout the 60-h

Table 1. Demographic characteristics (mean ± SD)

	Total	Bolus	PCA
n	16 (M8F8)	7 (M4F3)	9 (M4F5)
Age (years)	51.9 ± 8.8	55.4 ± 6.0	49.2 ± 9.9
Height (cm)	158.2 ± 8.3	157.7 ± 9.7	158.5 ± 7.7
Weight (kg)	57.6 ± 9.0	59.8 ± 8.6	56.0 ± 9.5
%VC	111.2 ± 12.8	107.4 ± 11.4	114.2 ± 13.6
$FEV_{1.0\%}$	80.0 ± 5.3	78.1 ± 4.1	81.6 ± 5.9
Total morphine dose (mg)	17.3 ± 3.6	17.4 ± 5.2	17.2 ± 2.2

PCA, patient controlled analgesia; M, male; F, female; %VC, percent vital capacity; $FEV_{1.0\%}$, forced expiratory volume in 1 s.

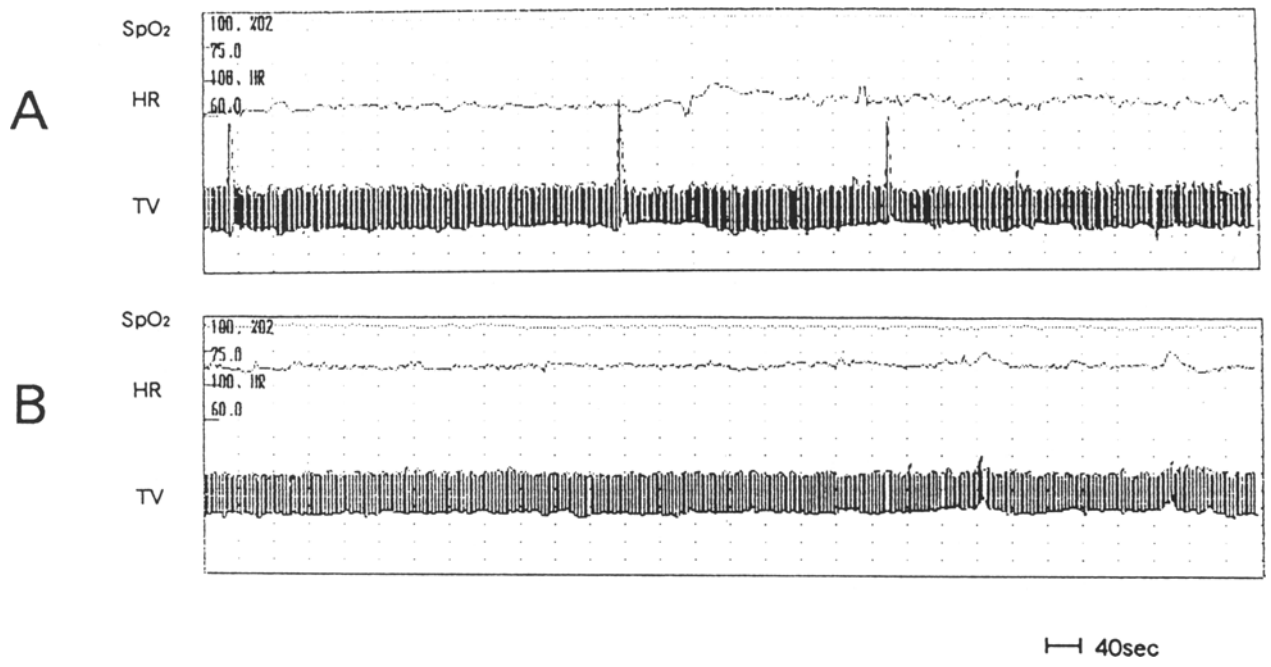

Fig. 1A,B. Representative breathing pattern during the preoperative monitoring period (**A**) and postoperative period (**B**) observed in a single patient receiving continuous epidural morphine with patient controlled analgesia (*PCA*). Note that postoperative breathing pattern is regular with no spontaneous deep breaths. HR, heart rate; TV, tidal volume; Spo_2, peripheral oxygen saturation

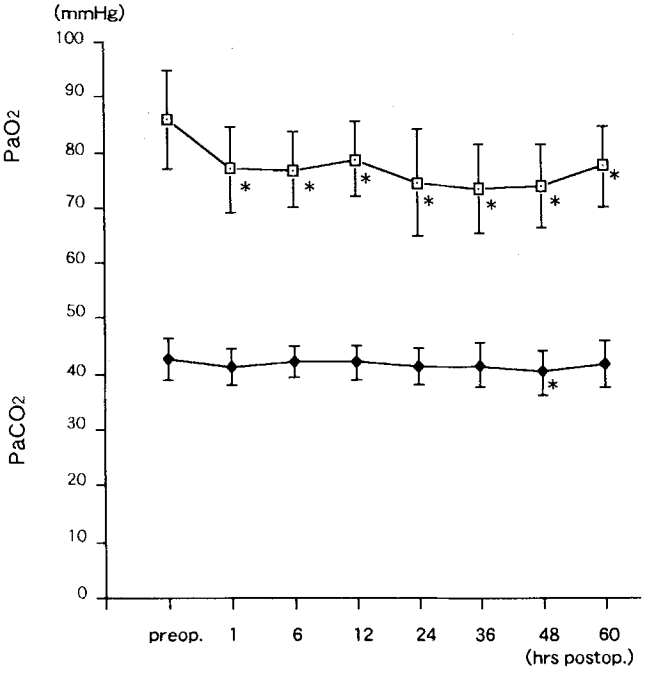

Fig.2. Mean (± SD) changes in Pao_2 (*open squares*) and $Paco_2$ (*closed diamonds*) in patients receiving epidural morphine for postoperative analgesia $*P < 0.05$ *vs* preoperative values. *preop.*, preoperative

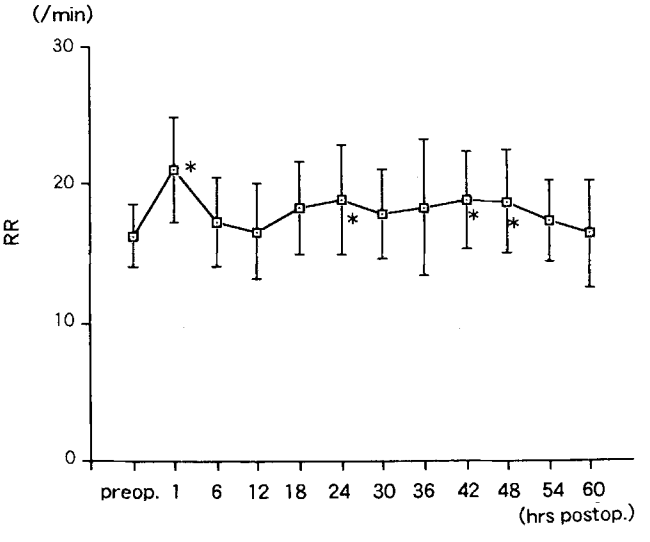

Fig. 3. Mean (± SD) changes in respiratory rates (*RR*) in patients receiving epidural morphine for postoperative analgesia. $*P < 0.05$ *vs* preoperative values. *preop.*, preoperative

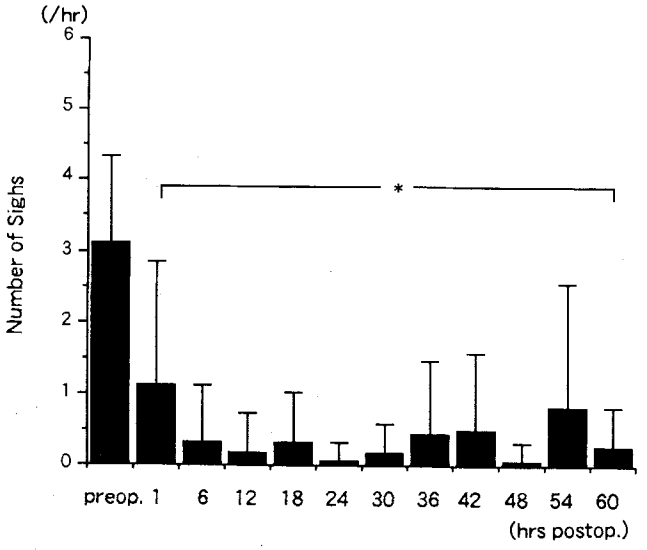

Fig. 4. Number of sighs (mean ± SD) observed preoperatively while asleep and postoperatively in patients receiving epidural morphine for postoperative analgesia. $^*P < 0.05$ *vs* preoperative values. *preop.*, preoperative

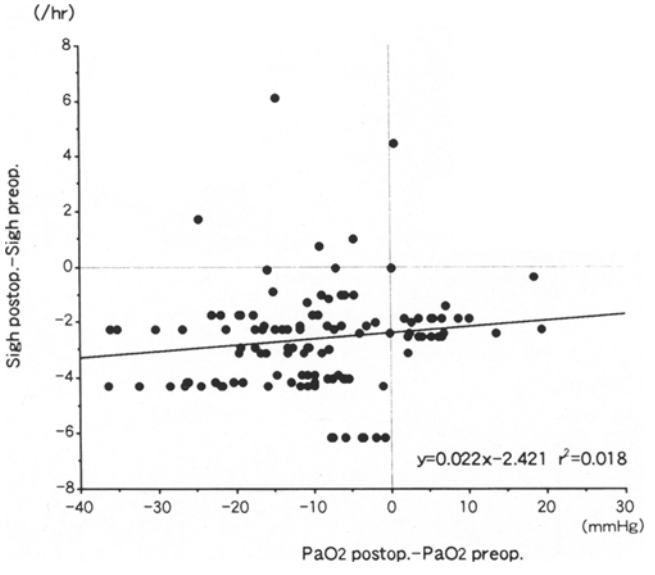

Fig. 5. Linear regression of analysis between the decreases in the number of sighs (y axis) and the decreases in Pao_2 values (x axis) observed postoperatively from the preoperative values in patients receiving epidural morphine for postoperative analgesia. The r^2 coefficient for the regression line is 0.018 ($P > 0.05$). No significant correlation was found between the decrease in sighs and the decrease in Pao_2. *preop.*, preoperative; *postop.*, postoperative

monitoring period on average (Fig. 4). Although both the mean number of sighs and the mean values of Pao_2 decreased postoperatively there was no correlation between them (Fig. 5).

Discussion

In this study, sighs were significantly depressed up to 60 h postoperatively in patients with epidurally administered morphine for analgesia after upper abdominal surgery. The majority of our patients showed no sigh at all, with an average frequency of less than one per hour. The reasons for this depression are not clear; however, two possibilities might be considered.

First, it is possible that large breaths and sighs might be inhibited by mechanical restriction of the chest wall. One of the earliest changes in postoperative ventilatory mechanics is known to be the marked reduction in vital capacity (VC) before any change in functional residual capacity (FRC) can be measured [7]. Due to the decreases in compliance and the alterations in lung volumes induced by the supine position, a decrease was found in FRC at 16–24 h postoperatively [8]. These changes might well restrict a large expansion of the thoracic cage and the normal motion of the diaphragm, resulting in depression of deep breaths such as sighing. Postoperative pain and spasms of the respiratory muscle may also restrict breathing with suppression of large breaths or sighs. Fear and anxiety may aggravate the situation by causing rigid muscle contractions in an attempt to splint the operative sites. However, it is unlikely that the depression of sighs in the postoperative period was due principally to postoperative pain, since adequate pain relief was obtained in all patients in this study.

Another possible explanation for the depression of sighs is inhibition of reflex activity. Since reflexive sighs are known to increase in number with a decrease in pulmonary compliance such as pulmonary congestion [9] or from chemical stimuli such as hypoxemia and/or hypercapnia [10,11], it is expected that the frequency of sighs might well increase in the postoperative period. However, this was not the case in our study. Thus, there must be mechanisms that inhibit reflex activation of sighs in the postoperative period. Perhaps changes in the conscious state may play an important role in inhibition of the reflex activity. Young adults are known to sigh 9–10 times per hour while awake in a semi-sitting position [12]. Our patients, however, sighed on average 3–4 times per hour preoperatively. The difference in the frequency between awake and sleep state supports the notion that the frequency of sighs may be influenced by the conscious state.

Changes in conscious state due to the residual effects of anesthesia may be responsible for the depression of sighs in the immediate postoperative period; however, the long-term depression cannot be explained by the residual effects of anesthesia. Furthermore, it has been shown that spontaneous sighs occur in some patients anesthetized with isoflurane [13]. Therefore, the use of

isoflurane during the operation cannot be the primary factor responsible for the depression of sighs in the postoperative period.

Morphine is known to depress not only the ventilatory responses to hypoxia and hypercapnia but also the frequency of sighs [14]. There is evidence that the frequency of sighs in the postoperative period is depressed immediately after administration of intravenous morphine [15], presumably due to the direct depression of the central nervous system. Considering that epidural morphine exerts similar central depression, it seems reasonable to assume that epidural morphine can cause long-term depression of sighs in the postoperative period.

As it is known that continuous infusion of epidural morphine is associated with lesser adverse effects than bolus epidural morphine [16], the two regimens were compared for their effect on depression of sighs, but no difference was found between the groups with the present dose.

Disagreement exists as to the role of spontaneous sighs in maintaining normal lung mechanics and oxygenation. Periodic sighing, by providing periodic hyperinflation of the lungs, has been considered to be necessary for preserving lung compliance through recruitment of atelectatic alveoli and restoration of surface forces [1,12]. In contrast, the study of Fletcher and Barber [2] showed that spontaneous sighing was not followed by changes in lung mechanics or compliance. The recent study of Grim et al. [13] also showed that there was no correlation between frequency or volume of sighs, Pao_2, and $Paco_2$ in patients anesthetized with isoflurane although in some patients spontaneous sighs may function to help maintain arterial oxygenation. However, the simple extrapolation of their results may not be entirely valid for patients undergoing major abdominal surgery.

Considering that "stir up" programs that include voluntary deep breathing are of the most clinical importance for improving oxygenation in postoperative patients after major abdominal surgery [17], it is likely that sighs or deep breaths may function to help improve arterial oxygenation in the postoperative period. However, our study showed that there is no significant correlation between the depression of sighs observed in the postoperative period and the values of Pao_2, suggesting that the long-term absence of spontaneous sighs may not contribute to the long-lasting hypoxemia in the postoperative period.

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