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# *Effects of Interpleural Bupivacaine on Respiratory Muscle Strength and Pulmonary Function*

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***Background:*** **Several reports suggest that interpleural local anesthetics may have deleterious effects on respiratory function. The current study investigated the effects of interpleural bupivacaine on human respiratory muscles and lung function.**

***Methods:*** **Thirteen patients (55 ± 4 yr old) with normal respiratory function and scheduled for cholecystectomy entered the study before surgery. Respiratory parameters were compared before and after the interpleural administration of 20 ml 0.5% bupivacaine plus 1:200,000 epinephrine while patients were supine; we evaluated breathing pattern, dynamic and static lung volumes, airway conductance, maximal inspiratory pressures (at the mouth; at the esophagus [$Pes_{sniff}$]; at the abdomen [$Pga_{sniff}$]; and transdiaphragmatic [$Pdi_{sniff}$]), functional reserve (tension–time index) of the diaphragm, and maximal expiratory pressures (at the mouth; at the esophagus [$Pes_{cough}$]; and at the abdomen [$Pga_{cough}$]). Hemoglobin oxygen saturation by pulse oximetry, heart rate, and mean arterial pressure were continuously monitored.**

***Results:*** **Respiratory rate (15 ± 1 to 19 ± 1 breaths/min; $P < 0.01$) and heart rate (78 ± 3 to 83 ± 3 beats/min; $P < 0.01$) were slightly increased. Dynamic and static lung volumes, airway conductance, hemoglobin saturation, and the remaining breathing pattern parameters were unchanged. Regarding respiratory muscles, maximal inspiratory pressure at the mouth, $Pes_{sniff}$, and tension–time index of the diaphragm did not change. $Pdi_{sniff}$ decreased slightly (102 ± 10 to 92 ± 10 $cmH_2O$; $P < 0.05$) because of a change in $Pga_{sniff}$ (24.2 ± 7.4 to 18.4 ± 6.8 $cmH_2O$; $P < 0.05$). Maximal expiratory pressure at the mouth remained unaltered, but $Pga_{cough}$ decreased (108 ± 10 to 92 ± 8 $cmH_2O$; $P < 0.01$), and $Pes_{cough}$ showed a trend to decrease (92 ± 13 to 78 ± 10 $cmH_2O$; $P = 0.074$).**

***Conclusions:*** **In our experimental conditions, interpleural bupivacaine did not significantly change lung function or inspiratory muscle strength but induced a slight decrease in abdominal muscle strength. Although this effect was minimal, its clinical relevance needs to be evaluated further in patients with impaired respiratory function. (Key words: Anesthetics, local: bupivacaine. Anesthetic techniques: interpleural. Muscles, respiratory: physiology. Respiration: function tests.)**

INTERPLEURAL local anesthetics produce sensory blockade of the hemithorax and superior hemiabdomen. However, the extent and characteristics of the motor blockade and the effects on respiratory function have not been clearly established. The block may affect muscles innervated by thoracic nerves, including the external intercostal muscles, used during inspiration, and the internal intercostal and abdominal muscles, which are the main expiratory muscles.[1] On the other hand, the diaphragm, which is the main inspiratory muscle, is less likely to be blocked because the phrenic nerve travels in the mediastinum, remote from the posterior rib cage, where local anesthetics are located when administered with the patient supine.[2] However, a large part of the surface of the diaphragm is in apposition with the lower rib cage[1]; in this area, the muscle or the terminal branches of the phrenic nerve may be blocked by local anesthetics. Therefore, both inspiratory and expiratory muscles may be affected by interpleural anesthetics.

Studies in animals have shown that interpleural anesthetics induce blockade of the intercostal nerves[3] and dramatically decrease the electromyographic activity of the diaphragm.[4] It has also been reported that in humans, interpleural anesthetics can occasionally result in unilateral bronchospasm[5] or phrenic nerve paralysis.[6]

However, no studies have been specifically designed or performed to investigate the effects of interpleural anesthetics on respiratory muscle strength and pul-

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Fig. 1. Sequence of the study. BP = breathing pattern; FS = forced spirometry (dynamic lung volumes); DLco = carbon monoxide diffusion; SLV = static lung volumes; SGaw = airway conductance; RMF = respiratory muscle function; $Sp_{O_2}$ = hemoglobin oxygen saturation by pulsoximetry; HR = heart rate; MAP = mean arterial blood pressure.

monary function in humans. Th
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## Materials and Methods

### Patients

After Institutional approval and
healthy adults for whom the resu
tion tests were normal and wh
subcostal cholecystectomy we
cluded in the study. Subjects exc
abnormal chest anatomy; pleuro
monary or cardiac disease; morb
index > 35 $kg \cdot m^{-2}$)[7]; known
mellitus; coagulation disorders
pain.

### Catheter Placement

Patients received no preanesth
surgery and with the patient s
catheter (Perifix, Braun, Melsun
troduced through an 18-G Hus
noject, Sherwood Medical, Wes
dom). The needle was inserted i
space below the right scapular
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0.5% bupivacaine plus 1:200,0
administered to rule out intrava
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presence of pneumothorax. I
contrast was not used, for two re
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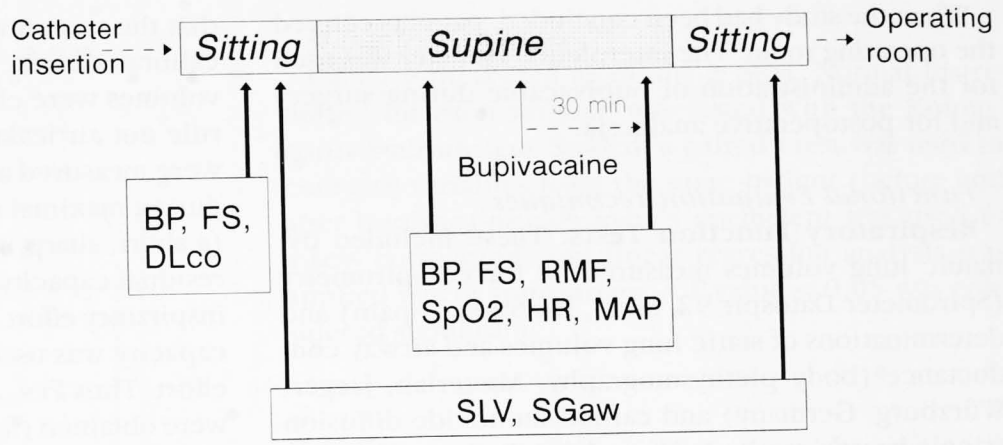


**Fig. 1. Sequence of the study. BP = breathing pattern; FS = forced spirometry (dynamic lung volumes); DLco = carbon monoxide diffusion; SLV = static lung volumes; SGaw = airway conductance; RMF = respiratory muscle function; $Sp_{O_2}$ = hemoglobin oxygen saturation by pulse oximetry; HR = heart rate; MAP = mean arterial blood pressure.**

monary function in humans. The current study investigated the effects of interpleural bupivacaine on human respiratory muscles and lung function.

## Materials and Methods

*Patients*

After Institutional approval and informed consent, 13 healthy adults for whom the results of respiratory function tests were normal and who were scheduled for subcostal cholecystectomy were consecutively included in the study. Subjects excluded were those with abnormal chest anatomy; neurologic, muscular, pulmonary or cardiac disease; morbid obesity (body mass index $> 35\ kg \cdot m^{-2}$)[7]; known drug allergy; diabetes mellitus; coagulation disorders; or acute or chronic pain.

*Catheter Placement*

Patients received no preanesthetic medication. Before surgery and with the patient sitting, an interpleural catheter (Perifix, Braun, Melsungen, Germany) was introduced through an 18-G Hustead-type needle (Monoject, Sherwood Medical, West Sussex, United Kingdom). The needle was inserted in the eighth intercostal space below the right scapular vertex, using the technique described by Scott.[8] The catheter was gently inserted and was then withdrawn so that the 10-cm mark could be seen on the skin surface. A test dose (3 ml 0.5% bupivacaine plus 1:200,000 epinephrine) was administered to rule out intravascular injection, and a radiographic control was performed to rule out the presence of pneumothorax. Interpleural radiologic contrast was not used, for two reasons: to avoid diluting or altering the distribution of bupivacaine and to prevent any possible effect of the dye on respiratory muscle function.

*Experimental Protocol*

Figure 1 describes the protocol used in this study. With the pleural catheter inserted and the patient sitting, breathing pattern, dynamic lung volumes (measured by forced spirometry), carbon monoxide diffusion, static lung volumes, and airway conductance were assessed.

The subjects were then placed supine, and 15 min later, breathing pattern, dynamic lung volumes, and respiratory muscle function were assessed. These parameters were again evaluated in the same position 30 min after administration of 20 ml 0.5% bupivacaine plus 1:200,000 epinephrine. To verify the extension and effectiveness of the analgesia, the pinprick test was performed, with the left hemithorax and superior hemiabdomen used as controls. The limits of cutaneous analgesia to be checked were as follows: cranially, a dermatome line between the clavicle and the nipple, related to the upper thoracic nerves[9]; caudally, the T10 dermatome related to the umbilical line[9]; and medially, the midline.

Static lung volumes and airway conductance were assessed after the interpleural blockade with the patients seated and were compared with the previous data obtained in the same position. They were not obtained in the supine position because plethysmography needed to be performed while the patient was sitting.

Hemoglobin saturation by pulse oximetry (Biox 3740, Ohmeda, Louisville, CO), heart rate, and noninvasive mean arterial blood pressure (Supermon 7210, Kontron Instruments, Milano, Italy) were monitored throughout the study. Patients breathed room air during the entire procedure.

When the study had been concluded, patients entered the operating room. The interpleural catheter was used for the administration of bupivacaine during surgery and for postoperative analgesia.

*Functional Evaluation Techniques*

**Respiratory Function Tests.** These included dynamic lung volumes measured by forced spirometry (Spirometer Datospir 92, Sibel, Barcelona, Spain) and determinations of static lung volumes and airway conductance (body plethysmography, Masterlab, Jaeger, Würzburg, Germany) and carbon monoxide diffusion (single-breath method, Masterlab). Reference values were those for a Mediterranean population.[10,11]

**Breathing Pattern.** Patients breathed through a mouthpiece and a two-way low-resistance valve (Hans-Rudolph, Kansas City, MO). Breathing pattern was obtained with a pneumotachometer (Screenmate, Jaeger) placed in the external inspiratory circuit. The flow signal was converted into a volume signal and registered with a multichannel recorder (R-611, Sensormedics, Anaheim, CA). Tidal volume, respiratory rate, minute ventilation, and inspiratory and total respiratory times were obtained from the recording. The system was calibrated at the beginning of each study. To ensure steady state, variables were evaluated after 5 min of quiet breathing.

**Respiratory Muscle Function.** Respiratory muscle function[12] was evaluated by determining maximal inspiratory and expiratory pressures measured at the mouth (PImax and PEmax, respectively), at the esophagus ($Pes_{sniff}$ and $Pes_{cough}$, respectively), and at the abdomen ($Pga_{sniff}$ and $Pga_{cough}$, respectively); transdiaphragmatic pressure (Pdi) was computed as Pga − Pes. The PImax was measured from the residual volume, and the PEmax was determined from total lung capacity. Both efforts were performed against a closed mouthpiece, by using the same manometer (Sibelmed 63, Sibel). The Pes and Pga were obtained with the classic two–balloon-catheter technique. The balloons (Jaeger) were the standard ones used to determine lung compliance. Each balloon's unstressed volume was 6 ml, and they were filled with the predetermined minimum air volume necessary to obtain the best recording. Thus, one balloon was placed in the esophagus and filled with 0.75 ml air, and the other was positioned in the stomach and filled with 1 ml. Each was attached to a pressure transducer (Transpac II, Abbot, Chicago, IL) that was connected to the above mentioned recorder. A pop test[13] previously performed confirmed that the system was critically damped. The system was calibrated at the beginning of each study, and balloon volumes were checked at the end of the procedure to rule out air leakage. Mean values of Pes, Pga, and Pdi were measured at tidal volume ($\overline{Pes}$, $\overline{Pga}$, and $\overline{Pdi}$) and during maximal respiratory efforts. The sniff maneuver (a short, sharp inspiratory nose effort from functional residual capacity) was chosen to evaluate the maximal inspiratory effort, and a voluntary cough from total lung capacity was used to evaluate the maximal expiratory effort. Thus $Pes_{sniff}$, $Pga_{sniff}$, $Pdi_{sniff}$, $Pes_{cough}$, and $Pga_{cough}$ were obtained (figs. 2 and 3). All measurements, except sniff and cough maneuvers, were performed using nose clips.

Maximal respiratory measurements (PImax, PEmax, forced spirometry, and sniff and cough measurements) were always conducted by the same physician and were randomly performed (with a standard random number table) to avoid interference from train-

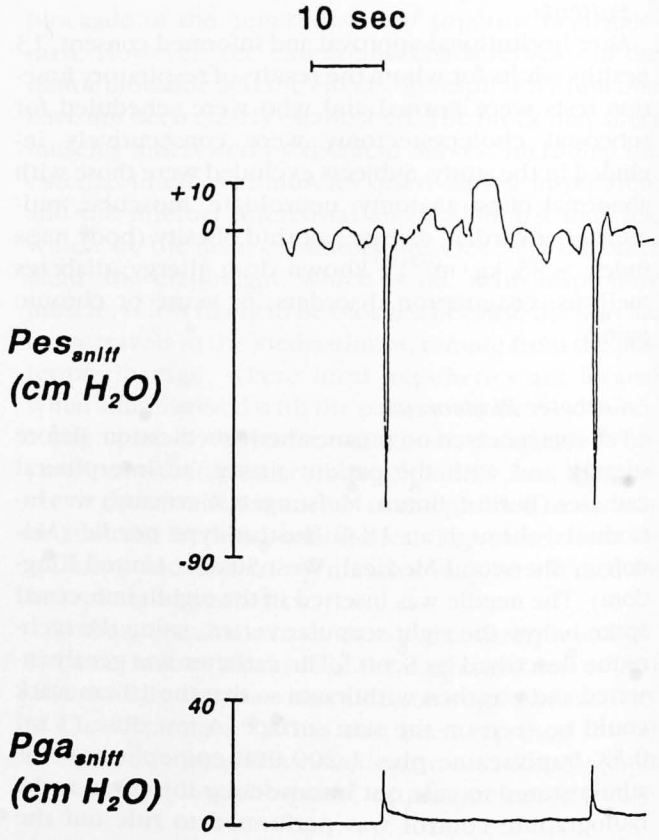


**Fig. 2. Individual recording of maximal inspiratory efforts. $Pes_{sniff}$ = maximal inspiratory pressure at the esophagus; $Pga_{sniff}$ = maximal inspiratory pressure at the abdomen.**





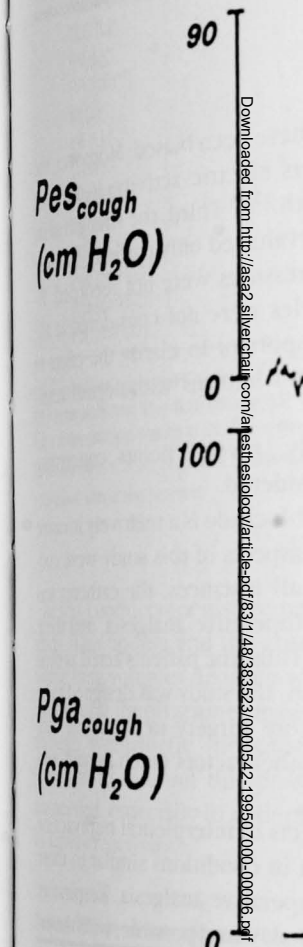


Fig. 3. Individual recording of ma
$Pes_{cough}$ = maximal expiratory pr
$Pga_{cough}$ = maximal expirator pres

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measurements was chosen in e
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curve with a semiautomatic
(Videoplan II, Zeiss, Kontro
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time. The speed of the recordi
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were calculated.

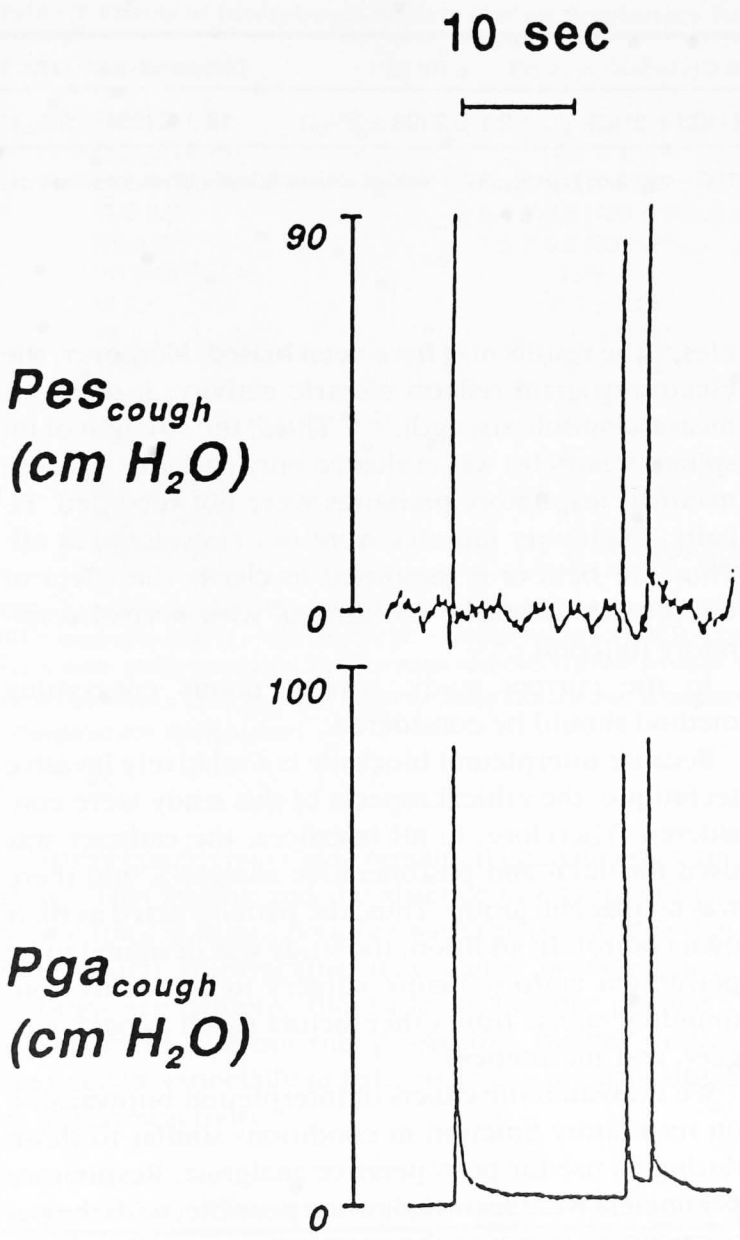


**Fig. 3. Individual recording of maximal expiratory efforts. $Pes_{cough}$ = maximal expiratory pressure at the esophagus; $Pga_{cough}$ = maximal expiratory pressure at the abdomen.**

ing or exhaustion. The best of three consecutive measurements was chosen in each case. $\overline{Pes}$, $\overline{Pga}$, and $\overline{Pdi}$ were calculated by measuring the area under their curve with a semiautomatic morphometric system (Videoplan II, Zeiss, Kontron Electronics Group, Eching, Germany), to obtain the mean pressure over time. The speed of the recording paper was increased to allow an easier measurement of the areas. After $\overline{Pdi}$ and $Pdi_{sniff}$ were measured, their relation ($\overline{Pdi}/Pdi_{sniff}$) and the tension–time index of the diaphragm ($\overline{Pdi}/Pdi_{sniff} \times$ inspiratory time/total respiratory time) were calculated.

*Statistical Analysis*

Data are presented as means ± SEM. Normal distribution for each variable was tested with the Kolmogorov-Smirnov test. Student's paired *t* test was used to compare variables from the same patient (before and after bupivacaine). Pearson's coefficient was used to assess correlation, and linear regression analysis was applied where appropriate. A $P$ value $< 0.05$ was considered significant.

## Results

Demographic data of the subjects are listed in table 1. As previously mentioned, respiratory function was normal in all subjects at the beginning of the study (table 2). Unilateral skin analgesia of the thorax and superior abdomen within the limits previously mentioned was obtained in all the patients, without evidence of analgesia on the left side.

After the administration of bupivacaine, dynamic and static lung volumes, and airway conductance were unaltered. An increase in respiratory rate without changes in the other parameters of the breathing pattern was observed; this change caused an increase in minute ventilation (table 3).

In the comparison of variables that express inspiratory muscle strength, no changes were detected in PImax and $Pes_{sniff}$. However, $Pdi_{sniff}$ exhibited a slight decrease, which was entirely attributable to a decrease in $Pga_{sniff}$; a positive correlation between changes in these two variables was obtained ($r = 0.84$; $P < 0.001$). Pes and Pga during quiet breathing ($\overline{Pes}$ and $\overline{Pga}$) as well as the functional reserve of the diaphragm against fatigue ($\overline{Pdi}/Pdi_{sniff}$, tension–time index of the diaphragm) remained unaltered (table 4).

Regarding expiratory muscle strength, no changes were observed in PEmax. In contrast, $Pga_{cough}$ significantly decreased, and a similar pattern was observed in $Pes_{cough}$ (table 4).

Heart rate significantly increased (78 ± 3 to 83 ± 3 beats/min; $P < 0.01$) whereas mean arterial blood

**Table 1. Demographic Data**

| Age (yr) | Sex (M/F) | Weight (kg) | Height (m) | Body Mass Index ($kg \cdot m^{-2}$) |
|---|---|---|---|---|
| 55 ± 4 | 1/12 | 69 ± 3 | 1.53 ± 0.02 | 29 ± 1 |

Values are mean ± SEM, where applicable.

**Table 2. Preoperative Respiratory Function Tests (Sitting)**

| FVC (L) | $FEV_1/FVC$ (%) | SGaw (1/kPa · s) | TLC (L) | RV (L) | $DL_{co}$ (mmol · min$^{-1}$ · kPa$^{-1}$) |
|---|---|---|---|---|---|
| 2.8 ± 0.2 (93 ± 3%$_{pv}$) | 80 ± 1.4 | 0.8 ± 0.06 | 4.4 ± 0.2 (103 ± 3%$_{pv}$) | 1.5 ± 0.2 (93 ± 8%$_{pv}$) | 18 ± 7 (104 ± 5%$_{pv}$) |

FVC = forced vital capacity; $FEV_1/FVC$ = forced expiratory volume in 1 s/FVC ratio; TLC = total lung capacity; RV = residual volume; SGaw = airway conductance; $DL_{co}$ = carbon monoxide diffusion; %$_{pv}$ = % of the predicted value.

Values are mean ± SEM.

pressure decreased (98 ± 4 to 90 ± 3 mmHg; $P < 0.01$) after interpleural bupivacaine. The hemoglobin saturation remained unchanged (97 ± 0.4 *vs.* 97 ± 0.5%) throughout the study.

## Discussion

The current study demonstrates that the administration of interpleural bupivacaine to healthy patients in the supine position has no deleterious effects on pulmonary function or inspiratory muscle strength. The possibility of respiratory impairment induced by interpleural anesthetics has been suggested by several groups of investigators.[4–6,14–19] In this situation, maneuvers such as coughing and sighing would be altered and could result in a greater rate of pulmonary complications in the postoperative period.

Although some studies have evaluated respiratory function after the administration of interpleural anesthetics,[16,19–22] they are not useful enough to address this issue. All of these studies used only forced spirometry, which is not an appropriate method to diagnose muscle weakness caused by nerve blockade.[12] In addition, they were performed in the immediate postoperative period, and their results may have been influenced by pain, residual anesthetics or the surgery itself. Moreover, results differ among these studies, maintaining the controversy.

In a study in dogs[4] assessing the effects of interpleural bupivacaine on respiratory muscle function, diaphragmatic electromyographic activity was markedly diminished. However, this report had several limitations. First, the validity of the model may be questioned: upper abdominal surgery, which can induce diaphragm dysfunction,[23] was performed. In addition, there are important differences between dogs and humans in anatomic position and thorax shape.[3] Second, because only the electromyographic activity from the costal diaphragm was measured and because the crural and costal diaphragm are considered two different muscles,[24] the results may have been biased. Moreover, the electromyogram reflects electric activity; it does not measure muscle strength.[12,25] Third, the strength of inspiratory muscles was evaluated only partially, because maximal inspiratory pressures were not recorded. Finally, expiratory muscles were not considered at all. Thus, we believe it important to clarify the effect of interpleural blockade on humans with normal respiratory function.

In the current study, several points concerning method should be considered.

Because interpleural blockade is a relatively invasive technique, the ethical aspects of this study were considered. Therefore, in all instances, the catheter was used for intra- and postoperative analgesia, and there was no placebo group. Thus, the patients acted as their own control. In addition, the study was designed to be performed entirely before surgery to avoid any confounding effects from other factors (such as pain, surgery, and anesthetics).

We evaluated the effects of interpleural bupivacaine on respiratory function in conditions similar to those during its use for postoperative analgesia. Respiratory parameters were recorded, when possible, with the patient supine, because the anesthetic is usually administered to supine patients, and patients remain supine in the postoperative period. Moreover, physiologic respiratory maneuvers (*i.e.*, cough) were used together with classic maneuvers. Finally, the volume and doses of local anesthetics were those most commonly used in clinical practice.

### *Analysis of Results*

Parameters from forced spirometry and static lung volumes did not change after interpleural bupivacaine. This finding is consistent with the hypothesis that there was no serious impairment in respiratory muscle function, although to support these results more specific indicators of respiratory muscle strength, such as maximal respiratory pressures,[12] were used.





**Table 3. Effects of Interpleural Bupiv**

| Parameter |
|---|
| FVC (L) |
| $FEV_1/FVC$ (%) |
| SGaw (1/(kPa · s))* |
| TLC (L)* |
| RV (L)* |
| RR (min$^{-1}$) |
| Vt (L) |
| VE (L) |
| Ti (s) |
| Ttot (s) |
| Ti/Ttot |
| Vt/Ti (L/s) |
| $\overline{Pes}$ ($cmH_2O$) |
| $\overline{Pga}$ ($cmH_2O$) |
| $\overline{Pdi}$ ($cmH_2O$) |

FVC = forced vital capacity; $FEV_1/FV$ = forc
RR = respiratory rate; Vt = tidal volu e; VE
$\overline{Pga}$ = mean gastric pressure at Vt; = me
Values are mean ± SEM. Student's ests fo
* Compared with sitting position.

Airway conductance also rema
study. This finding and the abs
namic lung volumes disagree w
interpleural bupivacaine may
through sympathetic blockade
However, to rule out this poss
are needed, especially in patien
to airway reactivity.

**Table 4. Effects of Interpleural Bup**

| Parameter |
|---|
| Inspiratory muscles |
| $PI_{max}$ ($cmH_2O$) |
| $Pes_{sniff}$ ($cmH_2O$) |
| $Pga_{sniff}$ ($cmH_2O$) |
| $Pdi_{sniff}$ ($cmH_2O$) |
| $\overline{Pdi}/Pdi_{sniff}$ |
| TTdi |
| Expiratory muscles |
| $PE_{max}$ ($cmH_2O$) |
| $Pes_{cough}$ ($cmH_2O$) |
| $Pga_{cough}$ ($cmH_2O$) |

$PI_{max}$ = maximal inspiratory pressure (at mou
transdiaphragmatic pressure; $\overline{Pdi}/Pdi_{sniff}$ = tra
$PE_{max}$ = maximal expiratory pressure (at mo
the predicted value; NS = not significant.
Values are mean ± SEM. Student's *t* tests fo

**Table 3. Effects of Interpleural Bupivacaine on Respiratory Function (Supine)**

| Parameter | Before Bupivacaine | After Bupivacaine | *P* Value |
|---|---|---|---|
| FVC (L) | 2.6 ± 0.2 (87 ± 3%$_{pv}$) | 2.5 ± 0.2 (84 ± 3%$_{pv}$) | NS |
| $FEV_1/FVC$ (%) | 80 ± 1 | 78 ± 2 | NS |
| SGaw (1/(kPa · s)* | 0.8 ± 0.06 | 0.7 ± 0.08 | NS |
| TLC (L)* | 4.4 ± 0.2 (103 ± 3%$_{pv}$) | 4.5 ± 0.3 (103 ± 2%$_{pv}$) | NS |
| RV (L)* | 1.5 ± 0.2 (93 ± 8%$_{pv}$) | 1.4 ± 0.2 (84 ± 9%$_{pv}$) | NS |
| RR ($min^{-1}$) | 15 ± 1 | 19 ± 1 | <0.01 |
| Vt (L) | 0.5 ± 0.05 | 0.48 ± 0.05 | NS |
| VE (L) | 7.6 ± 0.84 | 8.9 ± 1 | <0.05 |
| Ti (s) | 1.38 ± 0.08 | 1.24 ± 0.07 | <0.01 |
| Ttot (s) | 4 ± 0.3 | 3.3 ± 0.2 | <0.01 |
| Ti/Ttot | 0.35 ± 0.01 | 0.38 ± 0.01 | NS |
| Vt/Ti (L/s) | 0.37 ± 0.04 | 0.41 ± 0.05 | NS |
| $\overline{Pes}$ ($cmH_2O$) | −5.62 ± 0.69 | −5.23 ± 0.43 | NS |
| $\overline{Pga}$ ($cmH_2O$) | 1.7 ± 0.3 | 1.44 ± 0.22 | NS |
| $\overline{Pdi}$ ($cmH_2O$) | 7.32 ± 0.77 | 6.67 ± 0.51 | NS |

FVC = forced vital capacity; $FEV_1/FVC$ = forced expiratory volume in 1 s/FVC ratio; TLC = total lung capacity; RV = residual volume; SGaw = airway conductance; RR = respiratory rate; Vt = tidal volume; VE = expired minute volume; Ti = inspiratory time; Ttot = total respiratory time; $\overline{Pes}$ = mean esophageal pressure at Vt; $\overline{Pga}$ = mean gastric pressure at Vt; $\overline{Pdi}$ = mean transdiaphragmatic pressure at Vt; %$_{pv}$ = % of the predicted value; NS = not significant.

Values are mean ± SEM. Student's *t* tests for paired data are used to compare the parameters.

* Compared with sitting position.

Airway conductance also remained unchanged in our study. This finding and the absence of changes in dynamic lung volumes disagree with the hypothesis that interpleural bupivacaine may cause bronchospasm through sympathetic blockade in healthy persons.[5] However, to rule out this possibility, further studies are needed, especially in patients with a predisposition to airway reactivity.

With reference to inspiratory muscles, PImax and $Pes_{sniff}$ were unchanged after bupivacaine. However, $Pdi_{sniff}$, which specifically expresses the strength of the diaphragm, slightly decreased. This finding would indicate an impairment in the strength of this muscle. Nevertheless, the decrease in $Pdi_{sniff}$ was caused completely by a decrease in $Pga_{sniff}$, and this parameter reflects the abdominal pressure changes attributable to

**Table 4. Effects of Interpleural Bupivacaine on Respiratory Muscle Strength (Supine)**

| Parameter | Before Bupivacaine | After Bupivacaine | *P* Value |
|---|---|---|---|
| Inspiratory muscles | | | |
| $PI_{max}$ ($cmH_2O$) | −71 ± 7 (107 ± 10%$_{pv}$) | −67 ± 8 (99 ± 10%$_{pv}$) | NS |
| $Pes_{sniff}$ ($cmH_2O$) | −77.6 ± 5.2 | −73.6 ± 5.1 | NS |
| $Pga_{sniff}$ ($cmH_2O$) | 24.2 ± 7.4 | 18.4 ± 6.8 | <0.05 |
| $Pdi_{sniff}$ ($cmH_2O$) | 102 ± 10 | 92 ± 10 | <0.05 |
| $\overline{Pdi}/Pdi_{sniff}$ | 0.073 ± 0.005 | 0.079 ± 0.009 | NS |
| TTdi | 0.026 ± 0.002 | 0.029 ± 0.002 | NS |
| Expiratory muscles | | | |
| $PE_{max}$ ($cmH_2O$) | 104 ± 12 (74 ± 9%$_{pv}$) | 100 ± 13 (72 ± 10%$_{pv}$) | NS |
| $Pes_{cough}$ ($cmH_2O$) | 92 ± 13 | 78 ± 10 | 0.074 |
| $Pga_{cough}$ ($cmH_2O$) | 108 ± 10 | 92 ± 8 | <0.01 |

$PI_{max}$ = maximal inspiratory pressure (at mouth); $Pes_{sniff}$ = maximal inspiratory esophageal pressure; $Pga_{sniff}$ = maximal inspiratory gastric pressure; $Pdi_{sniff}$ = maximal transdiaphragmatic pressure; $\overline{Pdi}/Pdi_{sniff}$ = transdiaphragmatic pressure at Vt/maximal transdiaphragmatic pressure ratio; TTdi = tension-time index of the diaphragm; $PE_{max}$ = maximal expiratory pressure (at mouth); $Pes_{cough}$ = maximal expiratory esophageal pressure; $Pga_{cough}$ = maximal expiratory gastric pressure; %$_{pv}$ = % of the predicted value; NS = not significant.

Values are mean ± SEM. Student's *t* tests for paired data are used to compare the parameters.

the caudal displacement of the diaphragm. This decrease in $Pga_{sniff}$ may be related to increased abdominal compliance caused by the decreased motor tone. Because PImax and $Pes_{sniff}$ remained unaltered and both parameters evaluate the global inspiratory muscle strength,[26] changes in $Pdi_{sniff}$ may be considered irrelevant regarding inspiratory function.

The tension–time index of the diaphragm also remained unchanged. Thus, the risk of diaphragmatic fatigue is not increased in healthy adults receiving interpleural bupivacaine. However, these results cannot be extrapolated to cases of patients at increased risk of diaphragmatic fatigue, such as patients with severe chronic obstructive pulmonary disease.

Maximal expiratory maneuvers also suggested that there was a degree of motor blockade of the abdominal wall muscles, manifested as a decreased $Pga_{cough}$. Because abdominal expiratory effort is transmitted to the thorax, $Pes_{cough}$ showed a trend to decrease. This finding appears to be clinically unimportant in healthy subjects because the magnitude of the changes was small and because PEmax, which closely indicates the effective expulsive efforts performed with all the expiratory muscles, remained unmodified. However, these effects may be more important in patients with obstructive airways diseases, who frequently need the recruitment of abdominal muscles.

The increase in respiratory rate and minute ventilation after interpleural bupivacaine, without changes in the remaining parameters of the breathing pattern and hemoglobin saturation, was an unexpected result. It may be attributable to central ventilatory effects of the absorbed local anesthetic[27] or to the absorbed epinephrine. On the other hand, mean arterial blood pressure slightly decreased, perhaps because of the sympathetic blockade induced by bupivacaine[15,28] and the $\beta$-agonist effect of epinephrine,[29] which also may explain the increase in heart rate. None of these mechanisms could be confirmed in this study.

Our results demonstrate that the effects of interpleural bupivacaine on the respiratory system are minimal if given with the patient supine. However, when local anesthetics are given to patients in the lateral decubitus, a similar degree of analgesia is obtained,[2] but the safety of the technique in that position has not been clearly defined. In the lateral decubitus, the anesthetic spreads to the mediastinal pleural space,[2] where it may induce a blockade of the phrenic nerve, which is in contact with the mediastinal pleura.[30,31]

Finally, these results cannot be extrapolated to larger concentrations or volumes of bupivacaine or to continuous infusions.

In conclusion, interpleural bupivacaine, when administered preoperatively to healthy supine subjects, does not significantly impair lung or inspiratory muscle function. Bupivacaine produces a slight decrease in the strength of abdominal muscles, probably because of the motor block it induces. Although this impairment is small and does not reflect the effective expulsive pressures, its clinical relevance in the postoperative period remains unknown, especially in patients with respiratory or neuromuscular diseases.

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