Abdominal-muscle Rigidity Induced by Morphine and Nitrous Oxide

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Standard and integrated abdominal-muscle electromyograms and H reflex amplitudes of nine volunteers mechanically ventilated to maintain normal PaO₂, were studied. Morphine, 2 mg/kg, was given iv during ventilation with oxygen. One hour later 70 per cent nitrous oxide-30 per cent oxygen was substituted, and after another hour, six of the volunteers received thiopental, 3 mg/kg iv.

Morphine-oxygen increased abdominal-muscle activity and reduced H reflex amplitude by 3.0 per cent. Addition of nitrous oxide caused rigidity of the abdominal wall and reduced H reflex amplitude to 52 per cent of control. Addition of thiopental relaxed the abdominal muscles and reduced H reflex amplitude from 52 to 45 per cent of control. H reflex amplitude changes suggested that the abdominal rigidity was not caused by stretch reflexes or increased reflex excitability of spinal motoneurons, but probably resulted from a supraspinal effect of morphine and nitrous oxide. (Key words: Morphine; Nitrous oxide; Muscle rigidity; Electromyography; H reflex.)

Supplementation of nitrous oxide with narcotics is known to cause contractions of the abdominal muscles, often strong enough to produce a rigid abdominal wall and to lessen thoracic compliance.1-4 According to Sokoll et al.,2 the muscle rigidity results from the combined use of narcotics and nitrous oxide, but not from either agent alone. However, since these authors used rather large doses of narcotics without assisting respiration, their results could have been influenced by carbon dioxide retention.

During a study of the cardiovascular effects of large doses of morphine with and without nitrous oxide, we had the opportunity to measure by electromyography the abdominal-muscle activity brought about by these agents under conditions of constant PaCO₂. To test whether the muscle activity could result from hyperexcitability of the stretch reflex arc, we recorded the changes in amplitude of the H reflex, a spinal monosynaptic reflex evoked by electrical stimulation of the tibial nerve.

Methods

Nine healthy, unmedicated male volunteers (19-25 years old) were studied. Informed consent was obtained from every volunteer. Arterial blood pressure was continuously monitored with a strain gauge connected to a catheter placed in the brachial artery. PaO₂, PaCO₂, and pH were determined with appropriate electrodes.

Two monopolar needle electrodes, insulated except at their tips, were introduced 1 cm apart in the abdominal wall, at the level of the anterior axillary line, and advanced until signals heard from a monitoring loudspeaker during voluntary contraction of the muscles were maximal. The muscle action potentials were amplified, led to a Grass integrator, and displayed simultaneously with the integrator output on a double-beam oscilloscope.

The H reflex was elicited by stimulating the tibial nerve with single rectangular electrical pulses of 0.3-msec duration via two insulated wire electrodes introduced in the popliteal fossa until their bared tips lay close to the nerve. Stimuli were separated by no less than 30
seconds to allow for full recovery of reflex responses.\(^5\) Integrity of neuromuscular transmission was checked periodically by measuring the amplitude of the electrical muscle response to single supramaximal stimulation of the tibial nerve. The resultant action potentials of the calf muscles were recorded with two silver-silver chloride disc electrodes, diameter 8 mm, one placed on the skin over the lateral gastrocnemius muscle and the other over the Achilles tendon. The muscle action potentials were amplified and photographed from an oscilloscope.

The subjects lay supine throughout the study period, with their legs and feet supported to prevent changes in length of the calf muscles. Following 15 minutes of rest, all subjects were mechanically ventilated throughout the study at a constant tidal volume. A face mask was used in all cases, but after introduction of nitrous oxide most subjects needed intubation. Tidal volume and respiratory rate were adjusted initially to each subject's comfort and then kept constant. The flow of fresh gas into a circle system without soda lime absorption was adjusted to keep \(P_{\text{aCO}_2}\) near 40 torr. Body temperature, monitored with a rectal thermistor, was prevented from falling by use of blankets.

Control measurements of abdominal-muscle electromyogram (EMG), amplitude and latency of the H reflex, and integrity of neuromuscular transmission were made after the subjects became accustomed to mechanical ventilation with pure oxygen. Morphine, 2 mg/kg body weight, was then injected intravenously at the rate of 10 mg/min, and measurements were made 5, 10, 15, 30, and 60 minutes after completion of injection. The inhaled gas was then changed from oxygen to 70 per cent nitrous oxide–30 per cent oxygen, and the same sequence of measurements repeated. After one hour of nitrous oxide–oxygen, thiopental, 3 mg/kg body weight, was given iv to six subjects and followed by measurements at 1, 2, 5, and 10 minutes. Finally, the inspired gas was changed to pure oxygen and all subjects were given naloxone (average 0.04 mg/kg) intravenously to reverse the effect of morphine. Periodic measurements were continued until the subjects moved and dislodged the electrodes.

The peak-to-peak amplitudes in millivolts of the H reflex waves were measured on the photographs, and the value of the abdominal EMG integral was computed by averaging the tangent of its slope over a one-minute period. Statistical significance of the changes was analyzed by Student's t-test for paired data.

Results

During the control period four subjects had electrically silent abdominal muscles; the other five had small and variable degrees of activity, possibly related to physical discomfort and apprehension. In only one subject did the activity wax and wane rhythmically with the expiratory and inspiratory strokes of the ventilator.

Table 1 presents the means, standard deviations, and statistical significance of each group of observations, and figure 1 shows oscilloscope traces from a representative subject. During administration of morphine abdominal-muscle activity increased gradually in all subjects, to reach a plateau 10 minutes after completion of drug injection. Deviations from the plateau occurred only when the subjects talked or shifted position. The intravenous injection of morphine, 2 mg/kg, was conducive to light sleep, but did not cause unconsciousness. All subjects could be aroused easily, and at times they complained of itching or dryness of the mouth.

The degree of abdominal-muscle activity caused by morphine was significantly higher than that during control period, and the associated decrease in thoracic compliance necessitated an increase in airway pressure from a control value of 16 cm H\(_2\)O to 26 cm H\(_2\)O to restore tidal volume. Morphine had very little effect on the amplitude of the H reflex: at the end of drug administration the reflex had diminished by 30 per cent, showing no further change until the addition of nitrous oxide.

On changing from pure oxygen to 70 per cent nitrous oxide and 30 per cent oxygen all subjects lapsed into unconsciousness within 60 seconds. In the next 3 minutes the electrical activity of the abdominal muscles gradually increased eightfold, and the abdominal wall became "board-like." Six subjects could not be ventilated at all until an endotracheal
tube had been inserted with the aid of 60 mg succinylcholine. After intubation and recovery from the single dose of succinylcholine, the electrical activity and the rigidity of the abdominal muscles were as pronounced as before; adequate pulmonary ventilation required 32 cm H₂O airway pressure. The addition of nitrous oxide reduced the amplitude of the H reflex to 52 per cent of control within 10–15 minutes.

The administration of thiopental, 3 mg/kg, to six subjects who had been given morphine and nitrous oxide, quickly caused a drastic reduction in abdominal-muscle electrical activity and softening of the abdominal wall, accompanied by an increase in thoracic compliance, as reflected by an 8-cm H₂O fall of peak inspiratory pressure (fig. 1E). The effect of thiopental was short-lived, however, for in less than 10 minutes abdominal activity was again increasing. Thiopental also decreased the amplitude of the H reflex, although only from 52 to 46 per cent of control. The amplitude of the gastrocnemius EMG in response to supramaximal stimulation of the tibial nerve remained between 94 and 100 per cent of control throughout the study, indicating that neuromuscular transmission of single nerve impulses was essentially unchanged; the latency of the H reflex did not change.

Mean arterial blood pressures throughout the study ranged from a control value of 89 ± 2.3 to 84 ± 3.6 torr; the lowest Pao₂ was 113 torr; mean base excesses ranged from 1.4 ± 0.4 mEq/l after morphine to −0.7 ± 0.69 mEq/l during N₂O administration. Arterial CO₂ tensions are given in table 1. (A full account of the cardiovascular and metabolic changes will be reported elsewhere.)

From withdrawal of nitrous oxide to the time the subjects started moving, abdominal activity declined to a level somewhat lower than after administration of morphine, and the amplitude of the H reflex rose to 80 per cent of control. Dislodgement of the electrodes precluded further recording, but during the six hours or more that every subject remained under observation, palpation of the abdomen disclosed phasic expiratory muscle contractions present during sleep, but absent during arousal.

Discussion

The combined use of morphine and nitrous oxide for surgical anesthesia gives rise to strong contractions of the abdominal muscles. Under the conditions of this study, morphine itself in large doses caused only moderate abdominal contractions, and the inhalation of 70 per cent nitrous oxide alone has been shown to evoke a similarly weak response. Apparently, something about the combination of these two drugs causes a rigid abdominal wall and a decrease in thoracic compliance. Paco₂ deviations from normal were small and probably did not affect muscle rigidity (table 1). Thus, the findings reported by Sokoll et al. are likely to have resulted from adding nitrous oxide to the narcotic rather than from the presence of an elevated Pco₂.

Why the administration of morphine and nitrous oxide causes abdominal rigidity remains obscure. A direct drug effect on muscle fibers or on neuromuscular junctions seems unlikely because the rigidity affects only a specific

<table>
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<tr>
<th>Integrated abdominal</th>
<th>Nine Subjects</th>
<th>Six Subjects</th>
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<tr>
<td></td>
<td>Control</td>
<td>Morphine</td>
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<tr>
<td></td>
<td>0.036 ± 0.038</td>
<td>0.156 ± 0.077*</td>
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<tr>
<td>H reflex (mV)</td>
<td>5.37 ± 2.29</td>
<td>5.21 ± 2.26</td>
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<tr>
<td>Paco₂ (torr)</td>
<td>39.4 ± 3.3</td>
<td>41.8 ± 3.11</td>
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<td>pH</td>
<td>7.42 ± 0.03</td>
<td>7.40 ± 0.04</td>
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* P < 0.05.
Fig. 1. Left column, series of five H reflexes (second wave); right column, simultaneous integrated and standard EMG of the lateral abdominal-wall muscles. A, control; B, effect of morphine, 2 mg/kg iv; C, effect of adding 70 per cent N₂O; D, effect of adding thiopental, 3 mg/kg iv; E, partial recovery after withdrawal of N₂O. Note different calibrations of the standard EMG.
muscle group and the gastrocnemius–soleus response to single supramaximal stimulation of the tibial nerve remains unaltered.

Enhancement of stretch reflexes arising in the abdominal muscles is also unlikely, for it is well known that light surgical anesthesia abolishes the tendon reflexes, and our observations of the H reflex amplitude changes indicated that the reflex excitability of the spinal cord had decreased rather than increased. The H reflex is a spinal monosynaptic reflex equivalent to the ankle jerk, but differing from it in that it is elicited by electrical stimulation of afferent tibial nerve fibers originating in the muscle spindles, rather than by stretching of the muscle spindles themselves. The amplitude of the H reflex is a measure of the reflex excitability of spinal motoneurons in man.\textsuperscript{5, 8} Morphine reduced the H reflex minimally and caused moderate abdominal-muscle contractions, while the addition of nitrous oxide reduced the H reflex to 52 per cent of control amplitude and caused abdominal rigidity. Thiopental, on the other hand, had little further effect on H reflex amplitude but greatly reduced abdominal-muscle activity (table 1, fig. 1). Our observations thus imply that the reflex excitability of spinal motoneurons is not increased by morphine and nitrous oxide, and that the abdominal rigidity is unrelated to the degree of reflex excitability of spinal motoneurons.

The abdominal-muscle activity brought about by morphine–nitrous oxide probably originates at a supraspinal rather than at a spinal level. This hypothesis is supported by observations showing that the muscle activity decreases or disappears during hypobaric apnea and reappears when respiration resumes.\textsuperscript{9, 10} Another indication, though rather indirect, that the abdominal rigidity may originate at a supraspinal site is the drastic reduction of muscle activity we observed following administration of thiopental, a drug effective in arresting convulsions of supraspinal origin. Although thiopental reportedly suppresses the monosynaptic reflex in cats,\textsuperscript{11} the dose we used (3 mg/kg) barely affected the already depressed H reflex (table 1, fig. 1). Whatever its mechanism, the relaxing effect of thiopental on the abdominal muscles may have clinical application. During nitrous oxide–narcotic anesthesia for abdominal surgery, the judicious use of thiopental may decrease the need for muscle relaxants.

References