The Effect of Paralysis on Oxygen Consumption in Normoxic Children after Cardiac Surgery

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To determine whether paralysis reduces oxygen consumption (\( \dot{V}_{O_2} \)) after cardiac surgery in infants, the authors measured \( \dot{V}_{O_2} \) before and after paralysis in 17 sedated infants who were ventilated mechanically after cardiac surgery. Oxygen consumption was determined as being the difference between oxygen content of inspired and expired gases. The absence or presence of "movement" (breathing or repeated movement of the extremities) before paralysis was noted. For eight infants who did not "move" before paralysis, \( \dot{V}_{O_2} \) was similar before (9.1 ± 1.2 ml·kg\(^{-1}\)·min\(^{-1}\), mean ± SD) and after (9.0 ± 1.5 ml·kg\(^{-1}\)·min\(^{-1}\)) paralysis (\( p = 0.81 \)). However, for nine infants who did "move" before paralysis, \( \dot{V}_{O_2} \) decreased from 9.2 ± 1.4 ml·kg\(^{-1}\)·min\(^{-1}\) before paralysis to 8.0 ± 1.4 ml·kg\(^{-1}\)·min\(^{-1}\) after paralysis (\( p < 0.05 \)). One infant in each group had an increase in \( \dot{V}_{O_2} \) greater than 10% of the baseline value (i.e., 12% and 14%). In conclusion, if breathing or repeated movement is present before paralysis, paralysis decreases \( \dot{V}_{O_2} \) by 13% in sedated infants after cardiac surgery. If repeated or regular movement is not present before paralysis, paralysis does not decrease \( \dot{V}_{O_2} \). These data suggest that in normoxic patients, muscle paralysis does not significantly alter \( \dot{V}_{O_2} \) and therefore should not be used for this purpose. (Key words: Anesthesia: pediatric. Heart: congenital defects. Neuromuscular relaxants: pancuronium. Oxygen: consumption.)

Nondepolarizing muscle relaxants such as pancuronium commonly are administered to patients with severe lung disease who are being ventilated mechanically. For these patients, paralysis not only facilitates ventilation by eliminating struggling and unsynchronized breathing but also decreases the risk of pneumothorax.1-3 In neonates with hyaline membrane disease, paralysis improves arterial oxygenation.4,5 Paralysis also has been advocated in the postoperative management of infants following surgical repair of congenital heart disease in order to reduce oxygen consumption (\( \dot{V}_{O_2} \)). Although it is commonly believed that paralysis reduces \( \dot{V}_{O_2} \), this premise has been investigated only minimally in adults** and not at all in children. Therefore, we determined the effects of paralysis on \( \dot{V}_{O_2} \) in infants after cardiac surgery.

Methods

Patients

After obtaining approval from the Committee on Human Research, we studied 17 infants 10 days to 20 months of age. Sixteen studies were done within 8 h after cardiac surgery; one was done 48 h after surgery. No infant had respiratory insufficiency before surgery. All had definitive surgical repair of their cardiac lesions (transposition of the great vessels \( n = 6 \)), tetralogy of Fallot \( n = 3 \), atrioventricular canal \( n = 4 \), ventricular septal defect \( n = 4 \). During surgery, all infants were anesthetized with nitrous oxide plus halothane (\( n = 16 \)) or isoflurane (\( n = 1 \)) and were paralyzed with pancuronium. All infants underwent cardiopulmonary bypass. After surgery, all were ventilated mechanically with time-cycled, pressure-limited ventilators. Peak inspiratory pressures ranged from 20 to 30 cmH\(_2\)O, end-expiratory pressure was 5 cmH\(_2\)O, frequency ranged from 16 to 26 breaths/min, and the fractional concentration of inspired oxygen (\( \text{FiO}_2 \)) ranged from 0.6 to 1.0. Ventilator settings were not changed during the study. All patients were sedated with morphine, 0.1–0.3 mg/kg; two patients also received diazepam, 0.1 mg/kg. These drugs were administered at least 15 min before control measurements; no additional morphine or diazepam was administered until after the second set of measurements. Morphine and diazepam were given at the discretion of the attending physicians, and the amount and time of administration varied. None of the patients received catecholamines. Before the study, we documented full neuromuscular function by sustained leg lift8 or train-of-four response of ulnar nerve stimulation.9

PARALYSIS AND OXYGEN CONSUMPTION

TECHNIQUE AND APPARATUS

Oxygen consumption was determined as being the difference between oxygen content of inspired and expired gases. The oxygen content of expired gas was determined by making timed collections of expired gas and measuring its volume and oxygen concentration. The oxygen content of inspired gas was determined by measuring its oxygen concentration and calculating its volume from the expired volume and respiratory quotient.

Expired gas was collected through a nonrebreathing respiratory valve (#286-50, Sierra Engineering Co.) into a 3-l Neoprene® latex bag (fig. 1). This valve, inserted between the ventilator circuit and endotracheal tube, directed inspiratory gas to the patient and expiratory gas into the bag. A one-way valve was placed at the entrance to the bag to prevent loss of expired gas. After gas was collected in the bag, it was withdrawn through a stopcock into a calibrated glass syringe for measurement of volume. Samples of this gas were drawn into water-sealed glass syringes for analysis of oxygen concentration by mass spectrometry (Perkin-Elmer 1100®). Samples of inspiratory gas were withdrawn from the inspiratory limb of the ventilator circuit into water-sealed glass syringes and were analyzed for oxygen concentrations by mass spectrometry.

All components of this system were tested for accuracy. The oxygen concentration of gas samples in the water-sealed glass syringes varied an average of 0.13% over 2 h. The nonrebreathing valve and collection bag were tested by injecting gas of known volume and oxygen concentration through an endotracheal tube connector. Volume measurements varied less than 3% from the known injected volume. Oxygen concentration varied an average of 0.5% from the known injected concentration, even after gas had been stored in the bag for 2 h.

Inaccuracies in measurements due to loss of expired gas around the endotracheal tube or to fluctuations in \( F_{1O_2} \) were prevented. Loss of expired gas was prevented by using cuffed endotracheal tubes in 13 infants. In four infants, uncuffed endotracheal tubes were used; in these infants, we confirmed that there were no leaks around the tube by documenting the presence of only negligible concentrations of carbon dioxide in the posterior pharynx during expiration. To ensure that \( F_{1O_2} \) was kept constant, inspired gas was monitored continuously with an in-line polarographic monitor (Ohio Instrument Co.).

MEASUREMENT OF OXYGEN CONSUMPTION

Measurements, which were made in duplicate before and after paralysis, consisted of the following: 1) sampling of inspired gas; 2) two sequential timed collections (1–2 min each) of expiratory gas; 3) repeat sampling of inspiratory gas; 4) measurement of expired gas volume; and 5) sampling of this gas for later analysis of oxygen concentration.

After "before-paralysis" measurements were made, pancuronium (0.1 mg/kg) was given. Two subjects were given pancuronium (0.05 mg/kg) at the discretion of the attending physician. Twenty minutes later, the "after-paralysis" measurements were made. Then all gas samples were analyzed for oxygen concentration. Gases were kept in the Neoprene® bag for less than 20 min and in the glass syringes for less than 1 h.

With each set of measurements, we also recorded environmental and skin-surface temperatures, heart rate, and arterial blood pressure, \( pH \), \( P_{aO_2} \), and \( P_{aCO_2} \). We noted the presence or absence of shivering and "movement," which we defined as breathing or repeated movement of the extremities.

CALCULATIONS

Oxygen content was calculated from the following formula:

\[
\dot{V}_{O_2} = k[(F_{1O_2} \times \dot{V}_I) - (F_{EO_2} \times \dot{V}_E)]
\]

where

\[
\dot{V}_I = \dot{V}_E \frac{(1 - 0.15F_{EO_2})}{(1 - 0.15F_{1O_2})}
\]
had no change in $\dot{V}_{O_2}$, two had increases (2%, 14%), and four had decreases (1%, 6%, 6%, 14%) (fig. 2). The two subjects given pancuronium (0.05 mg/kg) were in this group; for both, $\dot{V}_{O_2}$ decreased (1%, 14%).

Nine patients "moved" before paralysis ("movement" group). For these patients, $\dot{V}_{O_2}$ was $9.2 \pm 1.4$ ml·kg$^{-1}$·min$^{-1}$ before paralysis and $8.0 \pm 1.4$ ml·kg$^{-1}$·min$^{-1}$ after paralysis ($P < 0.05$). Six patients had a decrease (10%, 14%, 19%, 24%, 24%, 58%), and three, an increase (2%, 6%, 12%).

These values for $\dot{V}_{O_2}$ were determined using a value of 0.85 for RQ. Using values for RQ ranging from 0.7 to 1.0, the magnitude and direction of change of $\dot{V}_{O_2}$ for each subject was consistent with that obtained with RQ equal to 0.85. In addition, we assumed that RQ remained constant during the period of the study.

Duplicate samples were obtained for all 34 measurements (i.e., measurements in 17 subjects before and after paralysis). In 3 of 34 instances, only one of the duplicate samples could be used due to technical errors. To test the reproducibility of the technique, we compared the two values for each of the 15 measurements after paralysis: measurements after paralysis should be more reproducible than those before paralysis because variability due to muscle activity has been eliminated. For 11 pairs the difference between individual measurements was less than 5%; for the other four pairs, the difference was less than 10%.

No patient had significant acidosis or hypotension (table 1); $\text{Pao}_2$ ranged from 76 to 350 mmHg. The difference in temperature between skin surface and environment changed more than 0.8°C in only one subject. For this subject ("no-movement" group), whose $\dot{V}_{O_2}$ did not change with paralysis, the difference between skin surface and environmental temperatures was 7.8°C before paralysis and 9.3°C after paralysis. Shivering was not observed in any of the subjects. Two patients had after-paralysis increases in heart rate that exceeded 10% (i.e., 11% and 23%); these were also the

### Table 1. Temperature, Heart Rate, and Blood Pressure Values for Infants Who Did and Did Not "Move"* before Paralysis

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Environmental Temperature (°C)</th>
<th>Difference between Skin Surface and Environment (°C)</th>
<th>Heart Rate (beats/min)</th>
<th>Systolic Blood Pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Movement&quot;</td>
<td>9</td>
<td>Before paralysis: 27 ± 2</td>
<td>7.2 ± 2</td>
<td>136 ± 20</td>
<td>99 ± 15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After paralysis: 27 ± 2</td>
<td>7.2 ± 2</td>
<td>138 ± 26</td>
<td>91 ± 19</td>
</tr>
<tr>
<td>&quot;No movement&quot;</td>
<td>8</td>
<td>Before paralysis: 27 ± 3</td>
<td>7.4 ± 2</td>
<td>139 ± 21</td>
<td>96 ± 14</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After paralysis: 27 ± 3</td>
<td>7.7 ± 2</td>
<td>145 ± 27</td>
<td>95 ± 15</td>
</tr>
</tbody>
</table>

Values are mean ± SD.

* "Movement" = breathing or repeated movement of the extremities.
only patients who had increases in \( \dot{V}_O_2 \) greater than 10% (14% and 12%, respectively).

**Discussion**

To our knowledge, no similar studies have been performed previously in infants, despite the common use of muscle relaxants to decrease \( \dot{V}_O_2 \). In this study, paralysis generally did not decrease \( \dot{V}_O_2 \) in sedated infants who did not “move” before paralysis. Oxygen consumption decreased variably in sedated infants who “moved” before paralysis. Oxygen consumption even increased in a few patients after paralysis, regardless of the presence or absence of movement before paralysis. It is notable that \( \dot{V}_O_2 \) after paralysis was similar for the movement and no-movement groups (\( P > 0.05 \) by Student’s \( t \) test for unpaired data). The lack of difference in values for \( \dot{V}_O_2 \) before paralysis most likely results from the variability of the data and suggests that movement before paralysis actually contributes little to oxygen consumption in these subjects.

Three groups have investigated the relationship between paralysis and \( \dot{V}_O_2 \) in animals or humans. In one study, \( d \)-tubocurarine did not decrease \( \dot{V}_O_2 \) in unsedated, normoxic, newborn lambs.\(^\text{12}\) When these lambs were made hypoxic, \( d \)-tubocurarine did decrease \( \dot{V}_O_2 \); however, \( d \)-tubocurarine decreased \( O_2 \) delivery (the product of cardiac output and arterial \( O_2 \) content) even more so, thereby creating an unfavorable balance between \( O_2 \) consumption and delivery. Likewise, in a second study, \( d \)-tubocurarine did not affect \( \dot{V}_O_2 \) in anesthetized dogs, although the depolarizing muscle relaxant succinylcholine did increase \( \dot{V}_O_2 \).\(^\text{13}\) In a third study, the only previous study performed in humans, \( d \)-tubocurarine was administered to five unsedated hypoxic adults who required mechanical ventilation for severe posttraumatic pulmonary insufficiency: \( \dot{V}_O_2 \) decreased in four subjects and increased in one.\(^\dagger\dagger\)

These studies appear to demonstrate a consistent finding: when subjects were hypoxic, paralysis may decrease \( \dot{V}_O_2 \); in contrast, when subjects were normoxic, as our subjects were, paralysis did not decrease \( \dot{V}_O_2 \).

Our results are consistent with what is known about the factors determining \( \dot{V}_O_2 \), and how we might expect paralysis with pancuronium to affect those factors,\(^\text{10,14}\) i.e., muscle activity, thermal environment (fever and ambient conditions), and secretion of catecholamines.

Pancuronium abolishes both voluntary muscle activity (movement) and involuntary muscle activity (resting tone and shivering). Abolishing voluntary muscle activity would be expected to decrease \( \dot{V}_O_2 \) variably, depending on the amount of muscle activity. We demonstrated that abolishing voluntary muscle activity with pancuronium in infants after cardiac surgery reduced \( \dot{V}_O_2 \) by an average of 15% ("movement" group). Abolishing involuntary muscle activity would be expected to have little effect on \( \dot{V}_O_2 \) in these infants because resting tone contributes little to \( \dot{V}_O_2 \) in infants,\(^\text{15}\) and shivering, although it greatly increases \( \dot{V}_O_2 \) in adults,\(^\text{16}\) does not usually occur in infants under 10 kg.\(^\text{10}\) In fact, none of our patients were observed to shiver. We demonstrated that in patients who did not move ("no-movement" group), abolishing involuntary muscle activity did not decrease \( \dot{V}_O_2 \).

Throughout each experiment, we attempted to keep the thermal environment constant to minimize its effect on changing \( \dot{V}_O_2 \). We did this by maintaining constant environmental conditions, i.e., the use of blankets or radiant warmers was consistent during both sets of measurements. Also, the two sets of measurements were done with a minimal time interval (20–30 min), to minimize any naturally occurring changes in thermal environment (i.e., in ambient temperature, humidity, air currents, or body temperature). The environmental condition that correlates best with \( \dot{V}_O_2 \) in infants is the difference between skin-surface and environmental temperatures.\(^\text{17}\) The differences between these values were consistent in all but one study. The values for \( \dot{V}_O_2 \) obtained in this study are greater than those reported in normal infants in a neutral thermal environment but similar to those obtained in normal infants with environmental conditions analogous to those in our study.\(^\text{18}\) We are unaware of other data for \( \dot{V}_O_2 \) in infants following cardiac surgery. Our values may reflect the response of the infant to surgery and anesthesia; in addition, differences between skin-surface and environmental temperatures (table 1) exceed values for a neutral thermal environment.\(^\text{17}\) These differences may contribute to a higher value for \( \dot{V}_O_2 \).

The effect of pancuronium on secretion of catecholamines in our patients is not known. Catecholamines increase \( \dot{V}_O_2 \) by increasing the metabolic rate of many tissues of the body including heart, liver, and, in infants, brown fat.\(^\text{14}\) Transient (usually <15 min) increases in heart rate and arterial blood pressure have been observed in children following pancuronium administration.\(^\text{19}\) These increases have been attributed to catecholamine secretion or vagolytic effects.\(^\text{20}\) Nonetheless, our after-paralysis measurements were obtained at least 20 min after pancuronium administration, so that these transient changes in heart rate and blood pressure are not likely to have affected our results. We speculate that pance-
ronium may have an indirect effect on catecholamine secretion by producing anxiety in inadequately sedated patients. Although all subjects in this study received morphine, we did not control the degree of sedation. Two of our subjects had after-paralysis increases in $\dot{V}_{O_2}$ greater than 10%. They were also the only subjects who had increases in heart rate of greater than 10%. The combination of increased heart rate and increased $\dot{V}_{O_2}$ is consistent, with known catecholamine effects and may indicate inadequate sedation.

Sedation, in fact, does reduce oxygen consumption. In one study in critically ill adults, morphine decreased $\dot{V}_{O_2}$ by 9–21%. In another study in children undergoing cardiac catheterization, administration of a combination of meperidine, promethazine, and chlorpromazine reduced $\dot{V}_{O_2}$ by 34%. These values are markedly greater than the decrease in $\dot{V}_{O_2}$ that occurred with paralysis in either our “movement” (13%) or “no-movement” (1%) group and suggests that sedation may offer a greater advantage than paralysis in decreasing $\dot{V}_{O_2}$. In addition, the use of sedation rather than paralysis may be safer. If there is a malfunction or disconnection of the mechanical ventilator, the paralyzed patient would be unable to breathe, whereas the sedated patient should be able to breathe, even though the ventilatory response probably would be blunted.

In summary, the small reduction in $\dot{V}_{O_2}$ associated with paralysis results from a reduction in muscle activity and does not occur if muscle activity has been abolished by prior sedation. At the present time, our preferred drug regimen to minimize muscle activity and thereby reduce $\dot{V}_{O_2}$ in these infants is to administer a narcotic analgesic such as morphine and to supplement it as necessary with a sedative-hypnotic such as diazepam.

References