Cardiovascular-Respiratory Actions of Mephentermine in Mitral Stenosis and Its Effects on Pulmonary Function in Chronic Pulmonary Emphysema

By Frank Barbera, M.D., Gabriel G. Regalado, M.D., Rosa L. Changoey, M.D., and José C. Dominguez, M.D.

In recent years, numerous publications have appeared emphasizing the usefulness of mephentermine during various forms of anesthesia as a means of maintaining an adequate blood-pressure level. Lundy has employed mephentermine successfully as an effective antidote against narcotic drugs. Pharmacological studies of sympathomimetic drugs on pulmonary circulation have shown mephentermine to be a pulmonary vasodilator.

The object of the present study was to investigate the respiratory effects of mephentermine systematically, and to test in humans the cardiovascular actions of this drug on the pulmonary circulation, in view of the scant information existing at present on these actions in man.

Methods

The present study comprised two groups of patients.

Chronic Pulmonary Disease Group

This group included 14 patients, 12 of whom were suffering from chronic pulmonary emphysema with varying degrees of fibrosis. The remaining two patients had asthma. Complete spirometrical studies were performed in 11 of these patients, both in the semirecumbent and sitting-up positions, at rest, and were repeated after intramuscular administration of 23 mg. of mephentermine (total). Average body surface in this group was 1.63 M². Immediately after these studies were completed, an aerosol with a known bronchodilator (cyclopentamine) was given and the maximum breathing capacity was determined when its bronchodilator effects were considered to be maximal. A Collins 9-L. respirometer without valves was used for these studies.

Within the next 48 hours, a Cournand needle was inserted in the radial arteries of the 14 patients and left in place during a suitable stabilizing period. A control sample of a five-minute respiration was collected in a Douglas bag, measured in a Precision Wet Test Meter and discarded. When conditions of the patient were considered basal, an arterial-blood sample was obtained under anaerobic conditions, while the patient inspired room air through a Collins J-valve. Expired air was collected in a Douglas bag during a five- to six-minute period. The number of respirations was recorded in a timed kymograph. The differences between the control sample of ventilation and the ventilation obtained simultaneously with an arterial-blood sample ranged between 0.22 and 0.90 L. per minute. The same procedure was repeated 25 minutes after intramuscular injection of 23 mg. of mephentermine (total). These same studies were carried out in three “hospital normal” controls.

Arterial blood was analyzed for CO₂, O₂, and blood hemoglobin O₂ carrying capacity in the Van Slyke manometric apparatus. Arterial-blood pH was determined at room temperature and corrected to 37 C. with the Beckman GS pH meter. Arterial pCO₂ was obtained with the Singer and Hastings nomogram. Expired air was analyzed in the micro-Scholander apparatus, and physiological dead space determined using the Bohr formula, assuming arterial pCO₂ to be identical with alveolar pCO₂, and corrected by subtracting the dead space of the equipment.

Mitral Stenosis Group

This group included 25 patients suffering from mitral stenosis with varying degrees of pulmonary hypertension. Three of these patients had undergone mitral commissurotomy 8 to 12 months previously, but at the time of the present study, they had residual pulmonary hypertension and were included in this group. The patients were studied at rest and 25 to 30 minutes after administration of mephentermine during a right-heart catheterization. A placebo was given before mephentermine in approximately one-third of the...
patients. In nine cases, 23 mg. of mephentermine was administered intramuscularly, while in the remaining 16 cases, the drug was given by continuous intravenous drip at the rate of 0.017 mg./Kg./min. The average body surface in the nine patients in whom the drug was used intramuscularly was 1.43 M.². The description of the technique followed has been published. The results have been studied statistically by means of Student's t-test.

In a control group of three "normals," catheterization was carried out in a similar manner; mephentermine was given intramuscularly in two cases and by continuous intravenous drip in one. The "normal" group consisted of two cases of patent ductus arteriosus and one atrial septal defect, 8 to 14 months after successful corrective surgery. Pressures in the pulmonary circulation were normal pre- and postoperatively. Clinical and hemodynamic studies were normal in this group.

**Results**

**Normal Controls**

The results of spirometrical, pulmonary-ventilation, and arterial-blood studies are contained in figure 1 and tables 1 and 2.

Expiratory minute volume and frequency of respiration increased in all cases. Alveolar ventilation went up in four cases and oxygen consumption rose in five of six cases; however, tidal-volume changes were negligible. Both CO₂ tension and content in arterial blood decreased in four cases, while CO₂ elimination increased in four and physiological dead space decreased in four cases. The physiological dead space/tidal volume ratio decreased in three cases, while arterial-blood saturation decreased in five cases.

The circulatory effects obtained in the three normal controls during right-heart catheterization are reported in figure 2.

Cardiac output and work of the left and right ventricles increased in all three cases. Arteriolar pulmonary resistance and arteriovenous O₂ difference decreased in every case. Heart rate, pressure in the pulmonary and systemic circuits, and total pulmonary-artery resistance changes were variable.

**Chronic Pulmonary Disease Group**

**Spirometry**

Maximum breathing capacity increased after mephentermine administration and a further increase occurred after cyclopentamine aerosol given immediately after termination of spirometry in the first six cases (table 1). Insignificant increases occurred in the last five cases with mephentermine or aerosol.

It may be assumed that in patients with emphysema, whose maximum breathing capacity remains unchanged after cyclopentamine aerosol, a functionally irreversible airway obstruction is present. This frequently repre-
Table 1

<table>
<thead>
<tr>
<th>Case</th>
<th>Control</th>
<th>25 min. after mephentermine</th>
<th>After aerosol* (cyclopentamine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>18.4</td>
<td>23.0</td>
<td>42.0 Emphysema</td>
</tr>
<tr>
<td>2</td>
<td>20.8</td>
<td>24.3</td>
<td>23.3 Emphysema + asthma</td>
</tr>
<tr>
<td>11</td>
<td>60.0</td>
<td>65.0</td>
<td>71.8 Emphysema</td>
</tr>
<tr>
<td>3</td>
<td>20.6</td>
<td>35.2</td>
<td>47.3 Emphysema + fibrosis</td>
</tr>
<tr>
<td>5</td>
<td>5.3</td>
<td>3.4</td>
<td>16.6 Emphysema + asthma</td>
</tr>
<tr>
<td>10</td>
<td>80.5</td>
<td>93.4</td>
<td>110.0 Asthma, bullae + emphysema</td>
</tr>
<tr>
<td>9</td>
<td>22.8</td>
<td>22.9</td>
<td>23.4 Emphysema</td>
</tr>
<tr>
<td>4</td>
<td>18.3</td>
<td>19.0</td>
<td>19.6 Emphysema</td>
</tr>
<tr>
<td>6</td>
<td>16.9</td>
<td>15.2</td>
<td>19.0 Emphysema</td>
</tr>
<tr>
<td>7</td>
<td>38.6</td>
<td>37.0</td>
<td>40.6 Emphysema</td>
</tr>
<tr>
<td>8</td>
<td>28.3</td>
<td>27.0</td>
<td>27.3 Emphysema</td>
</tr>
<tr>
<td>Normal 1</td>
<td>152</td>
<td>135</td>
<td>— Normal</td>
</tr>
<tr>
<td>Normal 2</td>
<td>90.6</td>
<td>100</td>
<td>106 Normal</td>
</tr>
<tr>
<td>Normal 3</td>
<td>78.0</td>
<td>68.6</td>
<td>84.0 Normal</td>
</tr>
</tbody>
</table>

*Aerosol was given immediately after maximum breathing capacity was obtained after mephentermine.

Table 2

<table>
<thead>
<tr>
<th>Spirometry</th>
<th>Emphysema</th>
<th>Normals</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Mean difference</th>
<th>Average % of change</th>
<th>Mean difference</th>
<th>Average % of change</th>
<th>Mean difference</th>
<th>Average % of change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max breathing capacity</td>
<td>+ 3.53</td>
<td>+11.6</td>
<td>+ 7.0</td>
<td>+21.3</td>
<td>+ 4.2</td>
<td>+2.8</td>
</tr>
<tr>
<td>Vital capacity</td>
<td>−142.0</td>
<td>−3.9</td>
<td>−169</td>
<td>−6.4</td>
<td>+63.0</td>
<td>+1.5</td>
</tr>
<tr>
<td>Inspiratory capacity</td>
<td>+ 55.5</td>
<td>+4.4</td>
<td>+ 25.5</td>
<td>−2.1</td>
<td>+ 3.0</td>
<td>+0.5</td>
</tr>
<tr>
<td>Expiratory reserve volume</td>
<td>+ 35.0</td>
<td>+2.5</td>
<td>+ 39.0</td>
<td>+3.4</td>
<td>−98.0</td>
<td>−7.8</td>
</tr>
</tbody>
</table>

*Column (1) represents the result of the 11 cases presented in Table 1.

1A in Column (2), the patients with functionally irreversible airway obstructions have been eliminated (the last five cases).

Mephenetermine in Mitral Stenosis and Emphysema

sents permanent peribronchial anatomical fibrosis. There is a decrease in vital capacity, an increase in the "two-step" vital capacity, and a small increase in both expiratory reserve volume and inspiratory capacity (Table 2, column 1). If cases in which aerosol administration produced no significant increase in maximum breathing capacity are dropped, then the effects of mephenetermine become a moderate increase in maximum breathing capacity and a more pronounced drop in vital capacity (Table 2, column 2).

Pulmonary-Ventilation and Arterial-Blood Studies (Table 5)

There was a small increase in expiratory minute volume and alveolar ventilation, a decrease in physiological dead space and physiological dead space/tidal volume ratio, CO₂ tension and content in arterial blood, and an increase in frequency of respiration. The changes observed in tidal volume, O₂ consumption, CO₂ elimination, respiratory quotient, O₂ uptake, and CO₂ removal per liter ventilation were negligible. None of these changes was statistically significant.

Mitral Stenosis Group

Pulmonary-Ventilation and Arterial-Blood Studies

No significant difference was found whether the drug was used intramuscularly or by continuous intravenous drip. There was a pronounced increase in expiratory minute volume and alveolar ventilation. In the intramuscular group, one case of nine had a slight decrease in expiratory minute volume and alveolar ventilation. In the intravenous series, 2 of 16 cases had small drops in expiratory min-
Schematic representation of cardiovascular changes in three normal controls after mephentermine. Dots represent two cases in which the drug was used intramuscularly during right-heart catheterization, and X represents one case in which it was used by continuous intravenous drip at the rate of 0.017 mg./Kg./min. The distance from the vertical axis represents percent of change after mephentermine. (Q) cardiac output per minute; (A-V diff.) arteriovenous oxygen difference; (systemic resist.) total systemic resistance; (pul. art. mean pres.) pulmonary-artery mean pressure; (mean wedge pressure) pulmonary mean wedge pressure; (radial art. mean pres.) radial-arterial mean pressure; (work left vent.) work of the left ventricle against resistance; and (work right vent.) work of the right ventricle against resistance.

Circulatory Studies (Table 4)

The results obtained were similar when the drug was used intramuscularly or by continuous intravenous drip. Cardiac output increased, pulmonary-artery pressure decreased, pulse rate increased significantly, and wedge pressure increased in intramuscular cases, while it decreased very slightly in intravenous cases. Pulmonary resistances were decreased; total systemic resistance decreased in intramuscular cases, while it remained almost unchanged in intravenous cases. Systemic pressures and work of both ventricles were increased. Right-atrial pressures decreased in all but one case. All cases with abnormally high right-atrial pressure in the control period were reduced after mephentermine.

Discussion

The increase in maximum breathing capacity in emphysema cases after mephentermine demonstrates that mephentermine partly reverses existing bronchospasm. This interpretation is based on the observation that no increase in maximum breathing capacity occurred in normal controls or in patients in whom cyclopentamine also failed to produce a significant change. The fact that a further increase in maximum breathing capacity obtained when cyclopentamine aerosol was used.

In this case, CO₂ content in arterial blood fell from 47.97 volumes per cent to 32.05; pCO₂ dropped from 35.0 to 25.0 mm. Hg, and pH increased from 7.36 to 7.43. If this case were omitted from the statistical studies, the observed increase in expiratory minute volume and alveolar ventilation would become significant.

Frequency of respiration was significantly increased, with negligible changes in tidal volume. Physiological dead space and physiological dead space/tidal volume ratio were decreased. There was a significant decrease in CO₂ content and tension in arterial blood, a significant increase in O₂ consumption and CO₂ elimination, and in arterial-blood pH. Arterial-blood saturation changes were small and insignificant. Oxygen uptake and CO₂ removal per liter ventilation showed minimal and insignificant changes.
after mephentermine indicates that mephen-
termine action did not relieve the existing
bronchospasm completely.

Maximum breathing capacity depends on
many factors. The changes observed in these
patients with bronchospasm after mephenter-
mine and/or cyclopentamine are unlikely to
be due to an increase in the muscular force
available, or to neuromuscular coordination of
respiration. They are interpreted as being due
to a decrease in the resistance to air flow
through the tracheobronchial tree.

It is generally accepted that relief of bron-
chospasm determines an increase in maximum
breathing capacity and in vital capacity. In
this series, the “two-step” vital capacity in-
creased while the vital capacity decreased.
This was observed both in the semirecumbent
and sitting-up positions. The discrepancy be-
tween the “two-step” vital capacity obtained
from the sum of the inspiratory capacity and
the expiratory reserve volume and that of the
vital capacity recorded as a single measure-
ment indicates air trapping. Increased air
trapping after mephentermine may be due to
the partial relief of airway obstruction in non-
ventilated or poorly ventilated pulmonary
areas.

Mephentermine increased pulmonary ven-
tilation markedly in normal controls and in
mitral stenosis, in contrast to the minimal
increases obtained in emphysema patients.
This is particularly apparent when compari-
sion is made between the emphysema patients
and the mitral stenosis group, in whom the
drug was used by the same intramuscular
route and in the same total dose. The increase
in expiratory minute volume was brought
about by a significant increase in frequency
of respiration, with small variable changes
in either direction in tidal volume. Increases
in tidal volume were frequently associated
with corresponding increases in physiological
dead space in mitral stenosis. The increased
ventilation determined a reduction in both
CO₂ content and tension in arterial blood, and
these changes led to a significant increase in
arterial-blood pH. While the changes were
minimal in emphysema patients, they were in
the same direction. The difference in degree
of response may be related to different pul-
monary pathology in each disease, or to the
relatively smaller dose per Kg. given to the
chronic pulmonary disease group. Average
body surface in this group was 1.63 M², while
the average body surface in the mitral stenosis
group in which it was used intramuscularly
was only 1.43 M².

The CO₂ and pH changes in arterial blood
cannot explain the hyperventilation observed.
Both hypocapnia and alkalosis are known in-
hibitors of respiration; consequently, the sta-
tistically significant increase in O₂ consump-
tion and CO₂ production cannot be the cause
of the increased ventilation through a mecha-

ism of increased CO₂ tension and content in
arterial blood. Both CO₂ tension and content
were decreased and arterial blood pH was in-
creased at the time the increased ventilation
was measured. Particularly striking in some
normal controls and in mitral stenosis cases
was the decrease in arterial-blood pCO₂ asso-
ciated with hyperventilation.

A bronchodilator action of mephentermine

**Figure 3**

Mitral stenosis cases. Ordinates represent per
cent of change in expiratory minute volume.
Abscissas represent per cent of change in O₂
consumption. There is a grossly linear correlation
between the per cent of change in pulmonary
ventilation and the per cent of change in O₂
consumption. Regression line was drawn by the
“freehand” method. Eliminating one case with
a great increase in ventilation after mephenter-
mine, the correlation coefficient r = 0.49, P <0.05.
Table 3

Control Values Compared with Values Obtained Twenty-five to Thirty Minutes after Administration of Mephentermine

<table>
<thead>
<tr>
<th>Pulmonary emphysema (14 cases) Mephentermine 23 mg., I.M.</th>
<th>Mitral stenosis (9 cases) Mephentermine 23 mg., I.M.</th>
<th>Mitral stenosis (16 cases) Mephentermine 0.017 mg./Kg./min., I.V.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean difference</td>
<td>P</td>
<td>Average % of change</td>
</tr>
<tr>
<td>( \dot{V} ) (L./min.)</td>
<td>+0.18</td>
<td>—</td>
</tr>
<tr>
<td>( \dot{V}^* ) (L./min.)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>( \dot{V}_A ) (L./min.)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>( \dot{V}_A^* ) (L./min.)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>( V_B ) (ml.)</td>
<td>—7.8</td>
<td>—</td>
</tr>
<tr>
<td>( V_E/V_T )</td>
<td>—1.4</td>
<td>—</td>
</tr>
<tr>
<td>( f )</td>
<td>+0.2</td>
<td>—</td>
</tr>
<tr>
<td>( V_T ) (ml.)</td>
<td>—5.3</td>
<td>—</td>
</tr>
<tr>
<td>( CACO_2 ) (vol. %)</td>
<td>—0.21</td>
<td>—</td>
</tr>
<tr>
<td>( PACO_2 ) (mm. Hg)</td>
<td>—2.1</td>
<td>—</td>
</tr>
<tr>
<td>( \dot{V}_O_2 ) (ml./min.)</td>
<td>—5.3</td>
<td>—</td>
</tr>
<tr>
<td>( \dot{V}CO_2 ) (ml./min.)</td>
<td>—5.0</td>
<td>—</td>
</tr>
<tr>
<td>Respiratory quotient</td>
<td>0.0</td>
<td>—</td>
</tr>
<tr>
<td>pH</td>
<td>+0.01</td>
<td>—</td>
</tr>
<tr>
<td>( SAO_2 ) (%)</td>
<td>+3.2</td>
<td>—</td>
</tr>
</tbody>
</table>

Abbreviations are same as in figure 1.

Supporting data for tables 3 and 4 have been deposited as document number 6815 with the ADI Auxiliary Publications Project. A copy may be obtained by citing the document number and remitting $2.50 for photoprints, or $1.00 for 35-mm. microfilm. Advance payment is required. Make checks or money orders payable to: Chief, Photoduplication Service, Library of Congress, Washington 25, D. C.

*One case with a very large increase was omitted.
and its vascular effects improving the ventilation-perfusion relationships, and thereby decreasing the physiological dead space, could determine an increase in alveolar ventilation. However, such a mechanism would produce a consistent reduction of the physiological dead space and physiological dead space/tidal volume ratio, with or without an increase in expiratory minute volume or frequency of respiration, as has been shown to occur with xanthines.11,12 Physiological dead space was reduced in 4 of 6 normals, in 8 of 14 emphysema cases, and in 10 of 20 mitral stenosis patients. Physiological dead space/tidal volume ratio was reduced in 3 of 6 normals—in insignificantly in emphysema, but significantly in mitral stenosis. These changes, as well as those observed in both directions in arterial-blood saturation,13 are consistent with some peripheral drug action on ventilation-perfusion relationships.

It appears probable that mephentermine acts on the respiratory center producing hyperventilation. A central action on the vasomotor center, as well as a central excitatory effect, have been described as being due to this drug.14-16 The disproportionate increase in expiratory minute volume and frequency of respiration, in contrast with its moderate bronchiolar and circulatory effects, suggests a central action. A central stimulating action of mephentermine would satisfactorily explain the consistent hyperventilation and polypnea which results in a reduction in CO₂ content and tension in arterial blood and an increase in arterial-blood pH. When primary, these factors are known inhibitors of pulmonary ventilation. The fact that no important hyperventilation was observed in emphysema may be due to the relatively smaller dose employed, or may be related to altered mechanics of breathing existing in this disease, which would partly overcome the effects of central stimulation. The possibility that the respiratory center in emphysema is less sensitive to CO₂ than in normals or in mitral stenosis appears less likely, since only four cases of 14 had hypercapnia at rest.

The significant increase in O₂ consumption and CO₂ elimination in mitral stenosis and in five of the normal controls is noteworthy. Others have shown that mephentermine increases myocardial O₂ consumption17 and cerebral O₂ consumption.18 This action is similar to that of other sympathomimetic amines. In this study, the increase in O₂ consumption cannot be accounted for by the significant increase in heart rate alone,19 but may be due, at least in part, to the myocardial effects or the action on other organs of mephentermine. The grossly linear correlation between the percentage increase in expiratory minute volume and the percentage increase in O₂ consumption suggests that the increase in O₂ consumption is due to the increased work of the respiratory muscles (fig. 3). In pulmonary emphysema, where no significant increase in expiratory minute volume occurred, there was no significant increase in O₂ consumption.

Circulatory Effects (Mitral Stenosis), Table 4

Mephentermine significantly increased the heart rate in mitral stenosis and in two of three normal controls. This effect of the drug has been previously described in dogs with
Mitral stenosis. Ordinates represent per cent of change in arteriovenous oxygen difference after mephentermine. Abscissas represent per cent of change in cardiac output. Increases in cardiac output were usually associated with decreases in arteriovenous \( O_2 \) difference (area A) or with minor changes in arteriovenous \( O_2 \) difference (area B). Decreases in cardiac output were almost always due to an increase in arteriovenous \( O_2 \) difference (area C).

isolated supported hearts, and in dogs in which the vagi have been cut.\textsuperscript{17} In our cases, direct myocardial actions of mephentermine appear to predominate over those of reflex origin which occur in the intact dog\textsuperscript{17} and in humans.\textsuperscript{20} Additional evidence of direct myocardial effects of mephentermine is the statistically significant reduction in right-atrial pressure, previously demonstrated in the dog\textsuperscript{17} and the increase in cardiac output.\textsuperscript{5-21}

In the present study, cardiac output increased in all three normal controls (mean increase 22.6 per cent) and in the majority of mitral stenosis cases. It should be noted that in the nine cases in which the drug was used intramuscularly, the mean increase was 17.7 per cent, while in the intravenous series, the mean increase was one-half this amount. Although this difference is not statistically significant, it may be explained by the difference in heart rate observed in both groups. While mean increases in heart rate in the intramuscular group amounted to 6.8 per cent, the intravenous group showed a mean increase of 14.9 per cent. It is well established in severe mitral stenosis that increases in heart rate will reduce cardiac output; consequently, in our cases, the increase in cardiac output due to myocardial drug action would be limited by the associated increase in heart rate (fig. 4).

The effects on pulmonary-artery pressure were variable. The average mean pressure was insignificantly reduced after the drug. Increases in pulmonary-artery pressure, attributed to increased cardiac output, occurred in two normals, in three intramuscular- and five intravenous-administration cases of mitral stenosis. Increases in cardiac output associated with decreases in pulmonary-artery pressure were present in one normal, two intramuscular- and four intravenous-administration cases of mitral stenosis. Pulmonary vascular resistance was obviously decreased in this last group. A passive reduction of pulmonary vascular resistance associated with increased cardiac output cannot, of course, be eliminated.\textsuperscript{22}

Previous work\textsuperscript{5} indicates that mephentermine increases cardiac output and dilates pulmonary arteries. Our limited information on three normal controls is in agreement with this finding. Cardiac output increased and pulmonary arteriolar resistance decreased in all cases. With the limitations encountered in mitral stenosis, mephentermine lowered arteriolar resistance in most cases (13 of 19 in which it was determined). Particularly in the intramuscular series, where changes in heart rate were less conspicuous and cardiac-output changes appeared more pronounced, mean wedge pressure increased, as should be expected of a drug dilating pulmonary arterioles in mitral stenosis.\textsuperscript{23} In the intravenous group, results were probably complicated by the marked increase in heart rate. However, mean changes in wedge pressure showed a minimal decrease, associated with a more pronounced drop in arteriolar pulmonary resistance.

With few exceptions, systemic blood pressure rose as a result of mephentermine. Total systemic resistance decreased in the normals and in the intramuscular group, while in 10 of the 16 intravenous cases, it was reduced or remained approximately the same. These re-
Mephentermine in Mitral Stenosis and Emphysema

Table 4*

<table>
<thead>
<tr>
<th>Control Values Compared with Values Obtained Twenty-Five to Thirty Minutes after Administration of Mephentermine During Cardiac Catheterization</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mitrail stenosis (9 cases)</strong></td>
</tr>
<tr>
<td>Mean difference</td>
</tr>
<tr>
<td>Right-atrial mean pressure</td>
</tr>
<tr>
<td>Cardiac output (L./min.)</td>
</tr>
<tr>
<td>Arteriovenous difference (vol./L.)</td>
</tr>
<tr>
<td>Heart rate (beats/min.)</td>
</tr>
<tr>
<td><strong>Systolic pressure</strong></td>
</tr>
<tr>
<td><strong>Diastolic pressure</strong></td>
</tr>
<tr>
<td><strong>Mean pressure</strong></td>
</tr>
<tr>
<td><strong>Mean ‘wedge’ pressure</strong></td>
</tr>
<tr>
<td><strong>Total pulmonary resistance</strong></td>
</tr>
<tr>
<td><strong>Arteriolar pulmonary resistance</strong></td>
</tr>
<tr>
<td><strong>Radial artery:</strong></td>
</tr>
<tr>
<td><strong>Systolic pressure</strong></td>
</tr>
<tr>
<td><strong>Diastolic pressure</strong></td>
</tr>
<tr>
<td><strong>Mean pressure</strong></td>
</tr>
<tr>
<td><strong>Total systemic resistance</strong></td>
</tr>
<tr>
<td><strong>Work of left ventricle</strong></td>
</tr>
<tr>
<td><strong>Work of right ventricle</strong></td>
</tr>
</tbody>
</table>

*See second footnote to table 3.

Consequently, it appears that peripheral action of mephentermine in mitral stenosis is of importance in the determination of cardiac output. Increased cardiac output in normal controls and in patients with mitral stenosis is brought about both by myocardial stimulation, producing a better emptying of the ventricles through an increase in the myocardial contractile force, and by peripheral factors supplying an adequate venous return. Decreased peripheral blood flow severely limits the response of the heart, in spite of a significant myocardial action.

**Summary**

Mephentermine increased maximum breathing capacity in emphysema patients due to partial relief of existing bronchospasm. Small variations occurred in tidal volume, arterial-blood saturation, O₂ uptake and CO₂ removal per liter ventilation, and in respiratory quotient. There was an increase in expiratory minute volume, alveolar ventilation, frequency of respiration, O₂ consumption, CO₂ elimination, and arterial-blood pH; a decrease oc-
curred in physiological dead space, physiological dead space/tidal volume ratio, and CO₂ content and tension in arterial blood. These changes were marked in normal individuals and in mitral stenosis patients, in contrast to the minimal effects obtained in emphysematous cases. Bronchodilatation in emphysema, reduction of the physiological dead space and physiological dead space/tidal volume ratio, and changes in both direction in arterial-blood saturation as well as circulatory effects suggest that mephentermine affects the ventilation-perfusion relationships throughout the lung. The disproportionate increase in respiratory minute volume and frequency of respiration, while arterial-blood findings showed a significant decrease in CO₂ tension and a significant increase in pH, suggests an important central effect. In normal and in mitral stenosis patients, mephentermine produced an increase in heart rate, a decrease in mean right-atrial pressure, and an increase in cardiac output as a result of myocardial stimulation. Changes in pulmonary-artery pressure were variable. Pulmonary arteriolar resistance decreased in all three normal controls and in the majority of mitral stenosis cases, while wedge pressure changed very slightly. These changes are interpreted as pulmonary vasodilatation. Systemic pressure increased, while total systemic resistance decreased or remained essentially unchanged. Arteriovenous O₂ difference decreased in most cases with increased cardiac output, and vice versa. Increased cardiac output, associated with unchanged or falling systemic resistances and decreased arteriovenous O₂ difference, suggests vasodilatation with increased peripheral blood flow. The fact that systemic resistance increases slightly in some cases must mean that vasoconstriction with decreased peripheral blood flow occurred in other vascular areas as a probable compensatory reaction. These effects led to an increase in arteriovenous O₂ difference and a reduction in cardiac output.

Acknowledgment

The authors express thanks to Drs. O. Teurbe-Tolon, Thomas Hernandez, and José Faura for their help during these experiments.

References

Mephentermine in Mitral Stenosis and Emphysema


Cardiovascular-Respiratory Actions of Mephentermine in Mitral Stenosis and Its Effects on Pulmonary Function in Chronic Pulmonary Emphysema
FRANK BARRERA, GABRIEL G. REGALADO, ROSA L. CHANGSUT and JOSÉ C. DOMÍNGUEZ

Circ Res. 1961;9:1185-1195
doi: 10.1161/01.RES.9.6.1185

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1961 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/9/6/1185