The Effects of Intravenous Hexamethonium on Venous Pressure of Normotensive and Hypertensive Patients with and without Congestive Heart Failure

By ROBERT R. BURCH, M.D.

The response of atrial pressure, venous pressure, pulse and respiratory rates to intravenous hexamethonium in 38 selected patients was studied. The drug seemed more effective where vascular tone was greater. Increased venous tone was indicated in congestive heart failure. The possible useful role of intravenous hexamethonium as an adjunct in the treatment of congestive heart failure was concluded from the objective and subjective observations made.

The immediate effects of hexamethonium on venous pressure and congestive heart failure have been reported previously.\(^1\)\(^2\) There was a variable decline in venous pressure associated with some relief of dyspnea. Since the drug seemed to have possible therapeutic value in congestive heart failure, knowledge of the duration of action as well as the time course relationship of changes in venous pressure to arterial pressure, pulse rate and respiratory rate may be important. Since previous observations have been concerned principally with hypertensive heart disease with congestive heart failure, data on the response of patients with normal arterial pressure and elevated venous pressure are lacking.

**METHOD**

Thirty-eight patients grouped into four categories of study were hospitalized at the Charity Hospital and had been at bed rest for varying lengths of time before these observations were made. Ten of the subjects who were convalescing from various disease states were normotensive without congestive heart failure (table 1), nine were normotensive patients with congestive heart failure (table 2), 10 were hypertensive patients without congestive heart failure (table 3), and nine had hypertensive heart disease and congestive heart failure (table 4). In addition to bed rest, all of the patients with congestive heart failure were receiving therapy including digitalis, salt restriction, diuretics and, in some cases, nasal oxygen at the time of the study.

Venous pressure was measured in the median basilic vein by means of a saline manometer and all values were corrected to the phlebostatic level.\(^3\) All observations included measurements of venous pressure, arterial pressure, pulse and respiratory rates as well as the usual clinical observations including attention to gallop rhythm, pulsus alternans, basal rales and dyspnea. Several consecutive observations were made to establish a control or basal level and were repeated as often as possible during intravenous injection of hexamethonium and at hourly intervals thereafter until the venous pressure returned to the control level. Prior to, immediately following the injection of hexamethonium, and at the end of the observation, the magnitude of the hepatojugular reflux was recorded after pressure had been exerted on the right upper quadrant of the abdomen for one minute.

The rate of injection as well as the dosage administered was recorded. There was considerable variation in the dosage and the rate of administration, the latter being intermittent (tables 1–4, figs. 1–4).

**RESULTS**

The results are summarized for all four groups separately in tables 1 through 4 and figures 1 through 4.

In Normotensive Subjects without Congestive Heart Failure. In patients in this category as well as in those in the other three categories, there were essentially two types of responses to the intravenous injection of hexamethonium (table 1 and fig. 1). The response in 8 of the 10 subjects in this group (fig. 1a and table 1,
The average dose of hexamethonium was 22.3 mg. administered in an average of 15.4 minutes. Venous pressure declined 6.2 mm. H\textsubscript{2}O, arterial pressure declined 16.6/6.8 mm. Hg and pulse rate increased 7.4 per minute. There was no change in respiratory rate.
In normotensive patients with congestive heart failure. The response of four normotensive patients with congestive heart failure followed the pattern summarized by figure 2a and table 2, subject 12. There was a more marked and rapid fall in venous pressure than in arterial pressure with the pulse and respiratory rates remaining unchanged. With the fall in

![Graph](image-url)
venous pressure, the hepatojugular reflux was absent but returned when the venous pressure approached control level again. Both arterial pressure and venous pressure returned to the control levels within two hours. The other type of response summarized by figure 2b and table 2, subject 16, was observed in 4 patients. Here again, venous pressure began to fall before arterial pressure. The magnitude of the hepatojugular reflux was not diminished by the injection, and at the end of a 13-hour period arterial pressure had returned to the control level while venous pressure had failed to do so.

The average dose of hexamethionium was 10.1 mg. injected over a period of 7.7 minutes. Following intravenous administration of hexamethionium, there was a mean fall in venous pressure of 79 mm. Hg and a decrease in the magnitude of the hepatojugular reflux of 17 mm. Hg. The venous pressure returned to control levels in all cases with a mean value of 4.0 hours. The arterial pressure declined 38/17 mm. Hg and returned to control level sooner in some patients than did the venous pressure. There were no consistent changes in the pulse or respiratory rates.

**In Hypertensive Patients without Congestive Heart Failure.** The response of 10 patients in the hypertensive group without congestive heart failure is summarized by figure 3. Six patients presented the pattern shown in figure 3a and

![Fig. 3. The effects of intravenous hexamethionium in hypertensive subjects without congestive heart failure. (a and b) The blood pressure, venous pressure, pulse and respiratory rate in two hypertensive subjects without congestive heart failure, illustrating the two types of responses encountered in this group. The amount and rate of injection of hexamethionium is indicated.](image)

**Table 3.—Summary of the Clinical Data and Responses to Intravenous Injection of Hexamethionium in Ten Hypertensive Patients without Congestive Heart Failure**

<table>
<thead>
<tr>
<th>Sub. No.</th>
<th>Clinical state</th>
<th>Age (yr.)</th>
<th>Dose given (mg.)</th>
<th>Time for injection (min.)</th>
<th>Venous Pressure (mm. Hg)</th>
<th>Bl. P.</th>
<th>Change in (mm. Hg)</th>
</tr>
</thead>
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<td>20</td>
<td>Essent. hypertens.</td>
<td>53</td>
<td>25.0</td>
<td>20</td>
<td>122</td>
<td>0</td>
<td>76</td>
</tr>
<tr>
<td>21</td>
<td>Essent. hypertens.</td>
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<td>15.0</td>
<td>12</td>
<td>104</td>
<td>0</td>
<td>80</td>
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<td>22</td>
<td>Essent. hypertens.</td>
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<td>12.5</td>
<td>16</td>
<td>89</td>
<td>0</td>
<td>91</td>
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<tr>
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<td>17</td>
<td>104</td>
<td>0</td>
<td>70</td>
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<tr>
<td>24</td>
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<td>25.0</td>
<td>12</td>
<td>117</td>
<td>0</td>
<td>115</td>
</tr>
<tr>
<td>25</td>
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<td>25.0</td>
<td>24</td>
<td>55</td>
<td>0</td>
<td>51</td>
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<tr>
<td>26</td>
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<td>25.0</td>
<td>14</td>
<td>95</td>
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<td>76</td>
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<td>25.0</td>
<td>14</td>
<td>100</td>
<td>0</td>
<td>105</td>
</tr>
<tr>
<td>28</td>
<td>Essent. hypertens.</td>
<td>37</td>
<td>25.0</td>
<td>11</td>
<td>196</td>
<td>+9</td>
<td>132</td>
</tr>
<tr>
<td>29</td>
<td>Essent. hypertens.</td>
<td>14</td>
<td>25.0</td>
<td>13</td>
<td>125</td>
<td>0</td>
<td>132</td>
</tr>
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</table>

Mean..................22.8 15.3 107 0.9 93 0 +0.7 206/134 -47/19 +0.6 0
22.8 mg. administered over a period of 15.3 minutes. Venous pressure declined an average of 14 mm. Hg and arterial pressure declined an average of 47/19 mm. Hg. There was a slight increase in pulse rate of 6.6 per minute without a change in respiratory rate.

In Patients with Hypertensive Heart Disease with Congestive Heart Failure. Four of the nine patients with hypertensive heart disease and congestive heart failure responded with marked simultaneous fall in venous pressure, arterial pressure and pulse rate, with little change in respiratory rate (fig. 4a and table 4, subject 35). The hepatojugular reflux was absent following hexamethonium. At the end of a three-hour period, the venous pressure and the magnitude of the hepatojugular reflux had returned to the control level, but the arterial pressure and pulse rate remained at a lower level. The other type of response elicited in the other five patients is summarized by figure 4b and table 4, subject 38. Following administration of the drug there was also a marked fall in venous pressure and arterial pressure but no change in the magnitude of the hepatojugular reflux or pulse and respiratory rates. Venous pressure required over eight hours to return to control levels while the blood pressure had not returned to control levels in 20 hours.

The average dose of hexamethonium was 21 mg., injected over a period of 11 minutes. The decline in venous pressure averaged 85 mm. Hg and the hepatojugular reflux decreased 18 mm. Hg. The average time for the venous pressure to return to the control level was 3.5 hours. Arterial pressure declined an average of 44/26 mm. Hg and pulse rate was reduced 13.5 beats per minute. The respiratory rate changed insignificantly.

The Effects of Intravenous Administration of Hexamethonium on Dyspnea, Basal Rales, Pulsus Alternans, and Gallop Rhythm. Two of the nine normotensive subjects with congestive heart failure with a protodiastolic gallop rhythm had no change in the rhythm following injection of the drug. All nine subjects were dyspneic prior to injection, and all experienced considerable improvement in this symptom.

![Fig. 4](http://circ.ahajournals.org/)

**Fig. 4.** The effect of intravenous hexamethonium in hypertensive subjects with congestive heart failure. *(a and b)* The blood pressure, venous pressure, pulse and respiratory rate in two hypertensive subjects with congestive heart failure, illustrating the two types of responses encountered in this group. The amount and rate of injection of hexamethonium is indicated. The dotted lines indicate the magnitude of the hepatojugular reflux.
However, there was no dramatic objective change in respiration.

Among the nine patients with hypertensive heart disease with congestive heart failure, four had pulus alternans. The sign disappeared in two patients following administration of the drug, lessened in degree in one patient, and remained unchanged in the other patient. There were seven instances of protodiastolic gallop rhythm in this group. In three instances the rhythm disappeared following administration of the drug, and it was unaffected in the remaining four patients. Dyspnea was present in seven of the nine patients in this group prior to use of the drug. In the three patients (subjects 33, 35, 37) who had acute pulmonary edema, there was a dramatic decrease in dyspnea following the injection of hexamethonium. They were able to dispense with the use of oxygen shortly after administration of the drug. The remaining four patients who had dyspnea prior to the injections reported considerable improvement in this symptom. Those subjects in both the normotensive and hypertensive groups who reported relief of dyspnea had little change in respiratory rate, yet they appeared more comfortable and respiration was obviously accomplished with less effort.

**DISCUSSION**

It should be emphasized that the patients were grouped solely on the basis of hypertension and congestive failure. In the two groups of patients with failure, normotensive and hypertensive, there was considerable variation in the clinical state of the failure. The subjects had already received varying periods of bed rest and varying amounts of drugs before this study was conducted. Some of the patients were improving in their state of failure, others were apparently stable and others were progressively becoming worse. Since the state of the congestive heart failure influences electrolyte metabolism, extent of edema fluid, body weight and the initial venous pressure, it would be expected to have an effect on the results observed in these experiments. In fact, many of the discrepancies among observations on congestive heart failure reported in the past may have been due to a failure or inability to define precisely the state of the failure.

The total dose of hexamethonium administered as well as the time required for injection varied in these experiments. The drug was administered slowly to permit adequate observation of its effects. When definite effects were noted, administration of the drug was
stopped regardless of the dose administered up to that point. The maximum dose administered, regardless of the degree of response, was 25 mg. Thus, the dosage varied considerably and in a relatively unstandardized manner. It is also apparent that doses larger than 25 mg. might have increased the magnitude of the response or might have caused a response when none was observed with the maximum dose of 25 mg. used in these studies. It is interesting to note that the average dose of hexamethonium was about the same for all the subjects without failure and for the hypertensive group with failure. The average dose required to elicit a response in the patients with congestive heart failure and normal arterial pressure was approximately half that of the other groups. Only one patient in this group received as much as 25 mg. and one patient had a marked response to as little as 3.75 mg. The reason for this "increased sensitivity" in the normotensive subjects with congestive heart failure is not apparent. This type of reaction had been observed by others using hexamethonium and other vasodilating agents.\(^1,4,5\)

It is generally agreed that drugs and procedures which influence peripheral blood vessels exert the same influence on both the arteries and the veins.\(^6\) However, it was possible to select the patients in these experiments so that the effects of the drug could be observed when both arterial and venous pressure (tone) were normal, when the venous pressure was high and arterial pressure normal, when arterial pressure was high and venous pressure normal and when the pressures were elevated in both the arterial and venous sides of the circulation. By such a selection, it was possible to observe the effects of hexamethonium on the reactions of arteries and veins when either or both showed a disproportional increase in tone. In subjects who had normal arterial and venous pressures—therefore normal tone—(group 1), ganglionic blockade was without much effect. However, the degree and duration of its effect on the veins and arteries differed in two instances. In the normotensive subjects who had congestive heart failure with venous hypertension (group 2) the decline in arterial pressure was greater than in the normotensive patients without failure. The decline in venous pressure in the subjects of group 2 was considerably greater than that in patients of group 1 in both absolute values and in percentile levels. The decline in venous pressure in the subjects of group 2 was greater than the decline in arterial pressure which declined only slightly. Thus, although the arterial pressure was within the established limits of normal in these subjects with congestive heart failure, there was evidence of an increase in arteriolar and arterial tone when compared with the subject with normal arterial pressure but without failure.

In hypertensive subjects without heart failure (group 3) the decline in arterial pressure was comparable to the change in pressure in the hypertensive patients with congestive heart failure in both absolute values and percentile levels. However, in subjects of group 3 the decline in venous pressure was much smaller than that in those of group 4 with venous hypertension. It was also observed that the subjects in whom venous pressure was normal, there was relatively little change in venous pressure following hexamethonium, although the arterial pressure declined (group 3).

In all subjects in whom there was an increase in venous pressure, the effect on venous pressure was greater regardless of the state of the associated arterial pressure. It was, therefore, demonstrated that the effect upon the veins was greater when the venous tone was abnormally increased. Furthermore, hexamethonium resulted in different degrees of reaction in the arterial and venous sides of the circulation. Not only did the degree of reaction differ, but there was a variation in the duration of the effect on the venous and arterial pressures as evidenced by the fact that the return to the control level of either was independent of the other. The actual time required for the venous pressure to return to the base-line level varied considerably; in some instances return to this level was not accomplished during the period of observation.

Additional evidence of the action of hexamethonium on venous tone was available from
studies on the hepatojugular reflux. With normal venous tone, venous pressure in the arm responded to right upper quadrant pressure either by no change in pressure or a decrease, whereas when the venous pressure was elevated, the response consisted of a further increase in pressure. The effect of right upper quadrant pressure was noted before and after hexamethonium. In some instances, the absolute rise in venous pressure in the arm after right upper quadrant pressure was as great following hexamethonium but simply reached a lower maximal level. In other instances, this rise in venous pressure was interrupted by the use of hexamethonium. These variations may, in part, be due to the failure to standardize the procedure. However, the results do indicate that hexamethonium exerted a marked effect on the veins when their tone was abnormally increased.

Hexamethonium resulted in an impressive improvement in the clinical status of the patients in failure. All the patients in groups 2 and 4 were subjectively and objectively more comfortable following administration of hexamethonium, a response reported previously. In the few instances in which acute left ventricular failure was present (subjects 33, 35, 37), the clinical improvement was most dramatic. The pulmonary edema and dyspnea rapidly cleared, and there was a disappearance of the protodiastolic gallop rhythm and the pulsus alternans in two subjects. The pulse rate declined an average of 20 beats per minute. In three instances, the gallop rhythm disappeared immediately after injection of the drug. The duration of the effect on venous pressure, determined by the time required to return to the control level, varied from 1 to 13 hours or longer. In no instance was there an untoward reaction to hexamethonium in the dosage used. In some instances the pulse rate increased, in others it decreased and when auricular fibrillation was present there was no change. It was difficult to evaluate the effects of hexamethonium alone on the course of the failure as other therapy was already present.

**Summary**

These observations showed that hexamethonium lowers venous pressure in congestive heart failure and that the effect on the peripheral arteries, arterioles and veins was greatest where tone was highest. The duration of the effect on venous pressure varied from 1 to 13 hours or longer. These observations also indicate the possible value and role of hexamethonium in the management of congestive heart failure.

**Summario in Interlingua**

Vinti patientes sin insufficientia myocardiac, qui recipieva 22,5 mg hexamethonium per administration intravenose, exhibiva nulle significative cambiamento de pression venose. Le pression arterial decresceva 16/7 mg Hg in normotensivos e 47/19 mg Hg in hypertensivos. Dece patientes normotensive con insufficientia myocardiac, qui recipieva 21 mg hexamethonium, exhibiva un reduction del pression venose de 86 mm H2O e un reduction del pression arterial de 38/17 mg Hg. In nove patientes hypertensive con insufficientia myocardiac, qui recipieva 21 mg hexamethonium, le pression venose se reduciva per 74 mm H2O e le pression arterial per 44/26 mm Hg. Le refluxo hepatojugular in le majoritate del patientes con insufficientia myocardiac esseva abolite o reducete post le administration de hexamethonium. Le pression venose e le pression arterial retornava al nivello de controlo le un independent del altere. Omne le patientes con insufficientia myocardiac monstrava meliorationes symptomatic. Le observationes monstrava que le effecto del administration intravenose de hexamethonium esseva le plus grande in le casos in que le tono del vasos sanguinees esseva le plus alte. Le possibile uso de hexamethonium como adjuncto al tractamento de insufficientia myocardiac es indicate.

**References**


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