Cardiac Index during Intravenous Levarterenol Infusion in Man

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Cardiac indices were determined by the Stewart-Hamilton indicator-dilution method during intravenous infusions of levarterenol in 25 human subjects. The rate and duration of the infusion as well as the increase in arterial pressure and bradycardia were varied in order to study their influences on the cardiac index.

Despite the great interest in levarterenol (noradrenaline), there have not been many investigations concerning the effect of its intravenous infusion on the cardiac index in man. Studies which have used the physical methods of ballistocardiography and pressure pulse contour analysis are unanimous in indicating a decrease in the cardiac index, while those which have used the direct Fick and indicator-dilution method are not in complete agreement. Many variables, e.g., age of subjects, rate and duration of the levarterenol infusion, the percentage increase in arterial pressure and the degree of induced bradyecardia were present in the aforementioned investigations. The present study was undertaken as an attempt to delineate more clearly the influences of these variables. Cardiac indices during infusions of levarterenol were measured by the Stewart-Hamilton indicator method in 21 normotensive and 4 mildly hypertensive patients.

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Methods

Twenty-six successful procedures were performed on 25 patients from the Medical Wards of the District of Columbia General Hospital. Eighteen were male and 7 were female. One patient (S.B.) was studied during 2 different admissions separated by 4 months. The patients were not acutely ill and were hospitalized for other than cardiovascular disease. The 4 patients classified as "mildly hypertensive" had arterial blood pressures of 140/90, 140/95, 175/90, and 150/110. The average age of the patients was 41 (14 to 69) years.

The patients had been fasting for 12 hours. During this time barbiturates or sedatives were not administered except to 3 patients who received promazine hydrochloride. After local anesthesia with 1 per cent procaine a 17 gage thin-walled needle was placed in a femoral artery. A 20 gage needle was then inserted into one of the antecubital veins and kept patent by an infusion of 5 per cent dextrose in water administered at approximately 2 ml./min. Following insertion of the needles a period of 15 to 30 min. was allowed for the attainment of a more basal state. In approximately one quarter of the procedures an initial "dummy run" was necessary to alleviate the patient's apprehension. Immediately following the control cardiac index determination a levarterenol solution (4 $\mu$g./mg. of 5 per cent dextrose in water)* was substituted by means of a three-way stopcock. This substitution was carried out without the patient's knowledge. The infusion was started slowly at approximately 0.05 $\mu$g./Kg./min. and the rate gradually increased until the desired level of average arterial pressure increase (range 6 to 53 per cent) or decrease in heart rate (range 0 to 35 per cent) was reached. The infusion of levarterenol was allowed to continue at this rate for several minutes before the second cardiac index was performed. The rates of the infusion at the time of

*Levophed, levarterenol bitartrate solution.
TABLE 1.—Changes in Cardiac Index during Levarterenol Infusion

<table>
<thead>
<tr>
<th>Arterial pressure (mm.Hg)*</th>
<th>Heart rate (Beats/min.)</th>
<th>Cardiac index (L./M./min.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>During</td>
</tr>
<tr>
<td>Age</td>
<td>41</td>
<td>122</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>±14</td>
<td>±17</td>
</tr>
</tbody>
</table>

*Throughout this table the terms, before, during and after are in response to the noradrenaline infusion.
†These figures refer to 5 procedures.
‡Average arterial pressure. Diastolic + systolic divided by 2.

this second cardiac index were 0.06 to 0.34 μg./Kg./min. The number of minutes which elapsed between the beginning of the drug infusion and the second cardiac index varied from 7 to 23 min. In 4 patients a cardiac index was determined 20 to 30 min. after the infusion was discontinued. If premature contractions were detected by palpation of the radial artery or if the patients experienced untoward subjective symptoms (headache, chest pain) the procedure was immediately discontinued and the results discarded.

Indicators were injected in volumes of 2 to 3 ml. during approximately 2 seconds from in vitro calibrated syringes. Although several calibrated syringes were used during the entire study the same syringe was used throughout each procedure. Second-second samples were collected manually from the femoral arterial needle into heparinized tubes. In 24 procedures 131-HSA (human serum albumin) was used in a dosage of approximately 20 μe. for each index determination. In one procedure Cr51 (Rachromate) was used in a dosage of approximately 75 μe. for each index determination; the Cr51 was given as labeled red cells prepared in standard fashion. In one procedure T-1824 (Evans blue dye) was used in a dosage of 10.05 mg. for each determination.

The radioactivity of both isotopes was counted in a well-type scintillation counter** from 1 ml. samples of whole blood. The optical density of the plasma samples containing T-1824 was measured by a spectrophotometer† at a wave length of 620 μν. Counts per minute per milliliter or optical densities were plotted on the ordinate and the time in seconds on the abscissa on semilogarithmic paper. The integral of the indicator-dilution curves was determined according to Lilienfeld and Kovach. The cardiac index in milliliter per minute was calculated by dividing the amount of indicator administered (counts per minute or optical density) times 60 by the integral of the indicator-dilution curve. When T-1824 was used the result of the foregoing calculation was divided by one minus the hematocrit.

Heart rate was determined by palpation of the radial artery at the wrist and arterial pressures measured with a sphygmomanometer. Arterial blood hematocrits were determined in Winthrop tubes.

RESULTS

The results of the 26 procedures are presented in table 1 and figure 1. There were no significant differences11 between the average cardiac indices before, during, and after the infusion of levarterenol. A cardiac index determination following the discontinuance of this infusion proved impractical in all but 5 of the procedures since the lengthened time of the procedure was frequently associated with obvious patient fatigue and anxiety.

The data of the 26 procedures were analyzed for correlations between the percentage differences in cardiac indices before and during levarterenol infusion and the following...
pat_client_age

Fig. 1. A summary graph showing the lack of correlation between the percentage differences in cardiac indices before and during levarterenol infusion and the age of the patient, percentage increase in average systolic and diastolic arterial pressures and the percentage decrease in heart rate.

variables: age, percentage, heart rate decrease, percentage increase in average arterial pressure, percentage increase in pulse pressure, percentage increase in diastolic pressure, percentage increase in systolic pressure, control (preinfusion) diastolic and systolic pressures, control (preinfusion) cardiac index, rate of infusion, and length of time the infusion was given prior to the cardiac index determination. No significant correlation was found.12

DISCUSSION

In the 26 procedures reported here there is no significant difference between the cardiac indices before and during intravenous infusion of levarterenol. These results are not in agreement with those investigators who have used physical methods to measure the cardiac index: they have all reported a significant decrease.1-3

The data from the 4 published studies in which the cardiac index was determined by the direct Fick method are in conflict. Both Goldenberg et al.4 and Patel et al.7 reported statistically nonsignificant changes in 9 and 21 patients respectively. However, Fowler et al.5 demonstrated a statistically significant decrease in 11 per cent in 10 patients and Mason16 showed a decrease of 22 per cent in 4 patients. Wilber and Brust8 determined the cardiac index in 12 patients by the indicator-dilution method (T-1824). Although control values were not reported, the cardiac indices during levarterenol infusion were within the normal range.

Many variables are present in the experimental situation under discussion. Our primary aim has been to define the relationship of some of these variables to the changes in cardiac index during levarterenol infusion. The data from the 26 procedures of this study as well as those of Goldenberg et al., Fowler et al.,5 and Patel et al.7 (whenever the necessary data were available) have been analyzed for correlations between the differences in cardiac index before and during infusion and the variables listed above. No significant correlation was revealed. The studies in which physical methods were used to determine the cardiac index have not similarly been analyzed since it was felt these methods were not as reliable as the direct Fick method. The study of Mason16 was considered too small to provide a useful comparison and that of Wilber and Brust8 did not report control values.

SUMMARY

Cardiac indices were determined by the Stewart-Hamilton indicator-dilution method during intravenous infusions of levarterenol in 25 human subjects. Despite variations in the rate and duration of the infusions, increases in average arterial pressure and degrees of bradycardia, no significant correlation was revealed between changes in these variables and those of the cardiac indices.

ACKNOWLEDGMENT

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SUMMARIO IN INTERLINGUA

Le indices cardiac de 25 subjectos human esseva determinate per medio del metodo de Stewart-Hamilton a dilution de indicator durante le infusion intravenose de levarterenol. Ben que variaciones del rapiditate e del duration del infusiones esseva introducite in le studio e ben que augmentos del tension medie arterial e del grados de bradycardia esseva notate, nulle significative correlation se revelava inter iste variabiles e le valores del indice cardiac.
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12. Ibid, page 82.
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