THE EFFECT OF ADRENALINE, NORADRENALINE AND HYPERTENSIN ON THE VASCULAR DISTENSIBILITY OF THE HAND

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SUMMARY

The distensibility of the capacity blood vessels of the hand was measured in eight normal subjects, before and during the administration of adrenaline, noradrenaline and hypertensin.

In all subjects the infusions of these vaso-active substances was associated with a decrease in distensibility of the capacity vessels. The clinical significance of these findings is discussed.

METHODS

The vascular distensibility of the hand was measured by comparing the increase in hand blood volume resulting from intermittent obstruction of the venous return from the hand with the associated increase in vascular distending pressure. This technique has previously been described in detail (Watson, 1961).

Hand blood flow was derived from the initial rate of increase of hand volume during a period of venous obstruction. Arterial blood pressure was measured by auscultation over the brachial artery of the opposite arm, using a standard mercury sphygmomanometer. Mean arterial blood pressure was calculated as the sum of the diastolic pressure and one-third of the pulse pressure (Wood, 1956).

Constant intravenous infusion of a pressor drug at a known rate was achieved with a power-driven syringe, delivering 1 ml/min through a fine nylon catheter introduced percutaneously into an antecubital vein. By this technique adrenaline was infused at 4 μg/min, noradrenaline at 2 μg/min, and hypertensin (Val., hypertensin II asp-β-amide, Ciba) at 2 μg/min.

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The investigation was supported by a grant from the National Fund for Research into Poliomyelitis and other crippling diseases.

Procedure.

After the apparatus had been set up no records were taken for analysis for half an hour, although within this time saline was infused at 1 ml/min, the pneumatic cuff occluded the venous return from the hand for 10 to 20 seconds every 20 to 30 seconds, and the arterial blood pressure was measured at intervals of 1 minute. Twenty consecutive records obtained during periods of venous obstruction within 8 to 10 minutes were then taken for analysis. Adrenaline was then substituted for the infused saline without the subject's knowledge, and given for 10 minutes. Saline was then substituted for the adrenaline and continued for at least 20 minutes. This procedure was repeated with noradrenaline. Finally, hypertensin was given. At no time was the subject informed of alteration of the infused substance. A minimum period of 20 minutes was allowed between consecutive drugs, which were always investigated in the order stated. Records were continually obtained throughout the periods of administration of drugs and in the intervening periods. Each series of experiments took about 2 hours.

Subjects.

Eight male subjects, aged 19 to 37 years were investigated. None had clinical evidence of disease of the respiratory or circulatory systems.

Presentation of results.

The increase in hand volume during venous obstruction was expressed graphically against the simultaneous increase in vascular distending pressure: these parameters were measured at intervals of 0.2 to 0.5 sec throughout the period of venous obstruction. A curve was obtained representing the vascular volume-pressure relationship of the hand during each period of venous obstruction; twenty consecutive records obtained
Vascular volume-pressure relationship of a typical subject:

- ○ during saline infusion;
- × during adrenaline infusion.

The horizontal line at 1.5 ml represents the hand volume at which the gradient of each curve was measured.

Vascular distensibility during adrenaline infusion expressed graphically against vascular distensibility during saline infusion. The line drawn has a slope of 45°. Each symbol represents a different subject.

Hand blood flow during adrenaline infusion expressed graphically against hand blood flow during saline infusion. The line drawn has a slope of 45°. Symbols as in fig. 1b.

Hand vascular resistance/100 ml tissue during adrenaline infusion expressed graphically against hand vascular resistance/100 ml tissue during saline infusion. The line drawn has a slope of 45°. Symbols as in fig. 1b.
under constant conditions were analyzed, and the volume-pressure relationships presented in this paper represent means of these values. The gradient of a curve expressing mean volume-pressure relationship represented change of hand volume resulting from change in vascular distending pressure, and was therefore equal to vascular distensibility. As the vascular volume-pressure relationship of the hand is curvilinear (figs. 1A, 2A, 3A) it is necessary to measure the gradient of the curve at a constant hand volume so that comparable values can be obtained under different circumstances. In all the results presented below vascular distensibility was measured as the slope of a tangent drawn to the volume-pressure curve at a constant hand volume 1.5 ml above the baseline hand volume, measured when the subject was receiving an infusion of saline.

The hand volume at which vascular distensibility was measured was therefore independent of changes in baseline hand volume resulting from the administration of vasoactive drugs and is indicated in figures 1A, 2A, 3A as a horizontal line.

The vascular resistance of each 100 ml of tissue of the hand was calculated as

\[
\text{Mean hand blood flow (ml/100 ml tissue/min)} = \frac{\text{Mean arterial blood pressure (mm Hg)} - \text{Baseline hand venous pressure (mm Hg)}}{\text{Vascular distensibility}}
\]

The results obtained in this investigation are summarized in table I.

<table>
<thead>
<tr>
<th>Parameter during administration of drug</th>
<th>Parameter preceding administration of</th>
<th>Adrenaline</th>
<th>Noradrenaline</th>
<th>Hypertensin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean arterial blood pressure</td>
<td></td>
<td>0.95</td>
<td>1.10</td>
<td>1.15</td>
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<tr>
<td>Vascular distensibility</td>
<td></td>
<td>0.70</td>
<td>0.55</td>
<td>0.50</td>
</tr>
<tr>
<td>Blood flow</td>
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<td>0.75</td>
<td>0.45</td>
<td>0.55</td>
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<tr>
<td>Vascular resistance</td>
<td></td>
<td>1.40</td>
<td>2.30</td>
<td>1.95</td>
</tr>
</tbody>
</table>

**RESULTS**

In all subjects a reduction in baseline volume occurred when the vasoactive drugs were given.

**Adrenaline.**

Figure 1A shows the change in vascular volume-pressure relationship of one subject, found when adrenaline was infused intravenously. This result is typical of six of eight subjects. A significant reduction (P<0.05) in vascular distensibility occurred. In the remaining two patients, although reduction was found it was not significant (P>0.05). The value for vascular distensibility found for each subject while receiving adrenaline is expressed graphically against the value found when the same subject received saline immediately before the administration of adrenaline (fig. 1B). In figure 1C the hand blood flow of each subject while receiving adrenaline is expressed graphically against the value found when the subject received saline immediately before the administration of adrenaline. A reduction of mean hand blood flow occurred in seven subjects, and no difference was found in the other subject. In figure 1D the vascular resistance of the hand of each subject while receiving adrenaline is expressed against the value found when the same subject received saline. A significant increase (P<0.05) in hand vascular resistance was found in five subjects. In the remaining three subjects the increase was not significant (P>0.05).

The vascular changes described commenced about 1 minute after the administration of the vasoactive drug began, and became constant after a further 2 to 3 minutes. When saline was substituted for the vasoactive drug the regression of vascular changes occurred at about the same rate. The changes in vascular resistance and in vascular distensibility occurred at the same time.

**Noradrenaline.**

Figure 2A shows the change in vascular volume-pressure relationship of one subject, found when noradrenaline was infused intravenously. This result is typical of all subjects. A highly significant reduction (P<0.01) in vascular distensibility was found. In figure 2B the value for vascular distensibility found for each subject while receiving noradrenaline is expressed graphically against the value found when the same subject received saline immediately before the administration of noradrenaline. In all subjects the reduction in distensibility was significant.
Vascular distensibility during noradrenaline infusion (ml/cm H$_2$O)

Hand volume increase (ml)

Vascular distensibility during saline infusion (ml/cm H$_2$O)

Hand blood flow during noradrenaline infusion (ml/100 ml tissue/min)

Vascular distending pressure (cm H$_2$O)

Hand blood flow during saline administration (ml/100 ml tissue/min)

The horizontal line at 15 ml indicates the hand volume at which the gradient of each curve was measured.

Vascular volume-pressure relationship of a typical subject:

Hand vascular resistance/100 ml tissue during noradrenaline infusion (mm Hg/ml/min)

Hand vascular resistance/100 ml tissue during saline infusion (mm Hg/ml/min)

Symbols as in fig. 2a.

Vascular distensibility during noradrenaline infusion is expressed graphically against vascular distensibility during saline infusion. Each symbol represents a different subject.
and highly significant in five (P<0.01). In figure 2c the hand blood flow of each subject while receiving noradrenaline is expressed graphically against the value found when the same subject received saline immediately before the administration of noradrenaline. A reduction of hand blood flow occurred in all subjects. In figure 2d the vascular resistance of the hand of each subject measured while receiving noradrenaline is expressed against the value found when the same subject received saline. A highly significant increase (P<0.01) in vascular resistance was found in all subjects.

Hypertensin. Figure 3a shows the change in vascular volume-pressure relationship of one subject found when hypertensin was infused intravenously. This result is typical of all subjects. A highly significant reduction (P<0.01) in vascular distensibility was found. In figure 3b the value for vascular distensibility found for each subject while receiving hypertensin is expressed graphically against the value found when the subject received saline immediately before the administration of hypertensin. In all subjects the reduction in vascular distensibility was highly significant (P<0.01). In figure 3c the hand blood flow of each subject while receiving hypertensin is expressed against the hand blood flow of the subject while receiving saline. A reduction in hand blood flow was found in all subjects. In figure 3d the vascular resistance of the hand of each subject measured while receiving hypertensin is expressed against the value found when the same subject received saline. A significant increase in vascular resistance (P<0.05) was found in all subjects, and this was highly significant (P<0.01) in seven of eight subjects.

The vascular changes described commenced about 1 to 2 minutes after the administration of hypertensin began and became constant at a further 2 to 3 minutes. When saline was substituted for hypertensin regression of the vascular changes occurred slowly over 10 to 15 minutes. The changes in vascular resistance and in vascular distensibility occurred at about the same rate.

DISCUSSION

The technique used in this investigation for measuring the distensibility of the capacity blood vessels of the hand is similar to that employed by Sharpey-Schafer (1961) for determining the distensibility of the capacity blood vessels of the forearm. It is related to the plethysmographic methods of measuring “venous” distensibility in vivo (Clark, 1933; Capps, 1936; Kidd and Lyons, 1958; Glover, Greenfield, Kidd and Whelan, 1958; Eckstein and Horsley, 1960), but enables changes in vascular distensibility to be followed with greater rapidity. It is known, however, that the value obtained for vascular distensibility varies with the rate of vascular distension: if the volume of the capacity vessels increases rapidly, then the pressure required to attain any particular volume is greater than if the volume-pressure relationships were examined during states of equilibrium (Alexander, 1948, 1954; Alexander, Edwards and Ankeney, 1953). Ideally, dynamic vascular distensibility measured under different circumstances should be measured at a constant rate of distension, that is, with a constant hand blood flow. As the vasoactive drugs also change the vascular resistance of the hand, this is not possible. This potential source of error cannot be the cause of the change in vascular distensibility observed in this investigation, for when adrenaline, noradrenaline or hypertensin was given the capacity vessels of the hand became less distensible (figs. 1b, 2b, 3b) although the rate of distension, or hand blood flow, decreased in all subjects. It is possible that the true decrease in vascular distensibility is greater than the measured increase.

Goldenberg and associates (1948) demonstrated that the intravenous administration of adrenaline caused a rise in systolic arterial blood pressure, little change in the diastolic blood pressure, moderate increase or no change in the pulse rate, great augmentation of cardiac output and significant increase in pulmonary vascular resistance. The total peripheral vascular resistance was reduced although the cutaneous resistance increased (Goldenberg et al., 1950). The results presented in this paper show that the increase in cutaneous vascular resistance is accompanied by a decrease in the distensibility of the capacity blood vessels of the hand. As most of the blood volume of the capacity vessels is contained in veins and venules (Litter and Wood, 1954), it is
Fig. 3A
Vascular volume-pressure relationship of a typical subject:
• during infusion;
× during hypertensin infusion.
The horizontal line at 1.5 ml indicates the hand volume at which the gradient of each curve was measured.

Fig. 3B
Vascular distensibility during hypertensin infusion expressed graphically against vascular distensibility during saline infusion. The line drawn has a slope of 45°. Each symbol represents a different subject.

Fig. 3C
Hand blood flow during hypertensin infusion expressed graphically against hand blood flow during saline infusion. The line drawn has a slope of 45°. Symbols as in fig. 3B.

Fig. 3D
Hand vascular resistance/100 ml tissue during hypertensin infusion expressed graphically against hand vascular resistance/100 ml tissue during saline infusion. The line drawn has a slope of 45°. Symbols as in fig. 3B.
probable that this altered vascular distensibility, measured at a constant hand volume, results from contraction of the smooth muscle of the vein wall.

Circulatory changes occurring when noradrenaline is infused have been described by Goldenberg and his colleagues (1950), and the circulatory responses to hypertensin by Daly and Duff (1960) and by Segel, Harris and Bishop (1961). The results obtained in this investigation indicate that the increase in arterial tone is probably accompanied by an increase in venous tone.

Under normal circumstances the capacity blood vessels may contain 60 per cent of the total blood volume (Landis and Hortenstine, 1950). Vasopressor drugs are used clinically to maintain an adequate arterial blood pressure when this is lowered by causes other than cardiac failure or reduction in blood volume. Under these circumstances, it is probable that clinical improvement observed with this treatment is a consequence not only of increase in peripheral vascular resistance, but also from reduction of distensibility of the capacity blood vessels. This would allow a given filling pressure for the right side of the heart, or transmural central venous pressure, to be lowered by causes other than cardiac failure or accompanied by an increase in venous tone.

The results obtained in this investigation indicate that the increase in arterial tone is probably accompanied by an increase in venous tone.

ACKNOWLEDGMENTS

I am greatly indebted to Dr. W. Ritchie Russell, Dr. J. M. K. Spalding, and Dr. A. C. Smith for research facilities, and to colleagues who acted as subjects for this investigation.

REFERENCES


BRITISH JOURNAL OF ANAESTHESIA

SOMMAIRE

Le degré de dilatation possible des vaisseaux de la main fut examiné chez huit sujets normaux avant et après administration d’adrénaline, de noradrénaline et d’hypertensine.

Chez tous ces sujets les infusions de ces substances vaso-actives étaient accompagnées d’une diminution du pouvoir de dilatation des vaisseaux volumineux. On discute de la signification de ces données.

ZUSAMMENFASSUNG


Bei allen Examindend gingen die Infusionen der genannten gefäßaktiven Substanzen mit einer Abnahme der Erweiterungsfähigkeit der Kapillargefäße einher. Die klinische Bedeutung dieser Befunde gelangt zur Diskussion.