Effect of Sympathomimetic Drugs in Acute Experimental Cardiac Tamponade

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The effect of Ammine and Wyamine on the depressed circulation in acute cardiac tamponade was studied in six dogs. As a result of tamponade, there was marked depression of the apparent right and left ventricular function curves which were then significantly re-elevated by the administration of these drugs. Evidence of coronary insufficiency was demonstrated in very severe tamponade where there was a low coronary perfusion gradient. The value of these drugs in acute clinical tamponade is suggested as a temporary expedient for maintaining an adequate coronary circulation until more definitive therapy can be initiated.

THE mechanism by which cardiac tamponade causes a circulatory disturbance was recently studied by Isaacs, Berglund and Sarnoff1 by means of ventricular function curves. They confirmed Starling's concept that the defect is a hindrance to diastolic expansion from the ventricles and not an inflow obstruction of the great veins as thought by Cohnheim and Beck.2 Since the basic circulatory defect is the restriction of diastolic fiber length and the consequent limitation of ventricular work,1 a pharmacologic agent which increases the force of ventricular contraction at any given fiber length or filling pressure and also increases peripheral vascular resistance might be expected to improve the circulatory status. Previous studies on the circulatory effects of Aramine (metaraminol) demonstrated that it does increase myocardial contractility and elevates peripheral vascular resistance.3, 4 The purpose of this communication is to report the results of the effect of this agent on the circulatory depression produced by acute cardiac tamponade.

METHOD

Six mongrel dogs weighing between 15.8 and 27 Kg. were anesthetized with morphine-chloralose-sulfate and maintained on positive pressure breathing with a Starling pump. Using the method previously described, systemic blood flow (cardiac output minus coronary flow), heart rate, aortic, pulmonary artery, right atrial and left atrial pressures were continuously recorded on a multichannel Sanborn Polyvisor recorder. All pressures were measured by strain gage pressure transducers; blood flow was measured by the Potter Electroturbimeter.5 Pulse rate was recorded with a Water's cardiotachometer. The anticoagulant used was heparin, 40 mg. /Kg. with an additional 120 to 180 mg. being given each hour after the initial dose. Ventricular filling pressures were raised by infusing whole blood from a reservoir connected to a femoral vein. Filling pressures were lowered by bleeding from the femoral artery into the reservoir. Stroke work for each ventricle was calculated6 over a wide range of filling pressures during a control period, after the production of cardiac tamponade, after the administration of a sympathomimetic agent while maintaining tamponade and following release of tamponade. Cardiac tamponade was produced by injecting an average of 104 ml. saline into the pericardial cavity through a rubber tipped polyethylene catheter that had been securely tied in place. In 1 animal, tamponade was produced by constricting the pericardium with sutures. Aramine (1-(1-(m-hydroxyphenyl)-3-amino-1-propanol) in doses of 0.05 mg. /Kg. body weight intravenously in all experiments except 1 in which Wyamine (N-methylphenyl-tertiary-butylamine sulfate) was given in a dose of 0.7 mg. /Kg. intravenously.

RESULTS

Acute Circulatory Effects of Cardiac Tamponade. In each experiment with the production of cardiac tamponade, there was a fall in systemic blood flow and aortic and pulmonary artery pressures together with a rise in right and left atrial pressures, and heart rate, as reported previously.1 Depression of Right and Left Ventricular

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Received for publication July 10, 1956.
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Function Curves by Tamponade and Effect of Aramine. Figure 1 shows the results. The apparent* depression of ventricular function curves is shown by the difference between curves I and II. The elevation of this depressed curve by 0.05 mg./Kg. of Aramine intravenously is shown by a comparison of curves II and III. A further elevation, as seen in curve IV, followed an additional 0.1 mg./Kg. of Aramine. Curve V was obtained after release of the tamponade and, in comparison with curve I, shows the effect of Aramine alone. Similar but not as pronounced results were obtained in the 1 experiment in which Wyamine was used.

Evidence for Coronary Insufficiency Resulting from Severe Tamponade. The tracing in figure 2 shows tamponade which was severe enough to reduce aortic pressure to a mean of 34 mm. Hg. This, despite subsequent small withdrawals of the pericardial saline, resulted in a progressive rise in right and left atrial pressures. It should be noted that although aortic pressure was 34 mm. Hg, right atrial pressure was 14 mm. Hg, thus producing an effective coronary perfusion pressure of only 20 mm. Hg.

**DISCUSSION**

Kuno,* found that adrenaline administered during tamponade of the heart increased arterial and slightly decreased venous pressure.
FIG. 2. Dog number 6; 20.5 Kg. Coronary insufficiency as manifest by further rise in atrial pressures during acute cardiac tamponade. At the first arrow, 110 ml. saline injected into the pericardial sac. At the second and third arrows, 20 ml. of saline were withdrawn, and at the fourth arrow, the remainder of the saline was withdrawn.

He attributed the improved heart function to a reduction in heart volume which would therefore lower the intrapericardial pressure. Cooley and Brockman found that norepinephrine produced a significant rise in blood pressure. Since 1-epinephrine had little effect on arterial pressure they attributed this to its vasoconstrictor action. In a previous study it was suggested that sympathomimetic substances which increase myocardial contractility might be of value in tamponade. The present experiments demonstrate that Aramine and Wyamine are effective agents in raising the depressed apparent right and left ventricular function curves under these circumstances. The administration of these agents is followed by a rise in aortic pressure, a larger stroke volume and a decline in heart rate. However, there is only a slight rise in cardiac output.

The mechanism by which vasopressor drugs improve the circulatory status in tamponade of the heart may not be entirely by means of vasoconstriction as was concluded by Cooley and Brockman, for the experiments demonstrate that the ventricles did more work for any given filling pressure after administration of Aramine or Wyamine, suggesting an increased myocardial contractility. Although there was a consistent slowing of the heart after the administration of Aramine, the increase in stroke work was not a function of this change in rate alone. Atropine was given to 1 dog together with Aramine during cardiac tamponade and there was a significant elevation of the ventricular function curves despite a faster heart rate.

In the 6 dogs studied in which severe tamponade was present, aortic pressure rose and heart rate slowed but cardiac output improved only slightly (4 to 37 per cent, average 13.5 per cent) after Aramine. Since end-diastolic volume is limited by severe pericardial tamponade, it is not to be anticipated that a more forceful myocardial contraction will greatly elevate cardiac output. Under these circumstances, only a limited volume of blood is available for ejection. This limitation is intensified by the slower heart rates after arterial pressures are elevated by Aramine.

The circulatory depression in severe cardiac tamponade is apparently sufficient to cause coronary insufficiency if effective coronary per-
Fusion pressure is reduced to levels inducing myocardial hypoxia. This view is supported by the progressively rising atrial pressures seen in figure 2, even though aortic pressure was 58/20 with a mean of 34 mm Hg. When coronary insufficiency occurs, right atrial pressure rises above the level induced by the tamponade alone and further lowers effective coronary perfusion pressure. The components of a vicious cycle are thus present. Under these circumstances, elevation of aortic pressure provides a higher effective coronary perfusion pressure and thus protects against myocardial hypoxia. In this way, arteriolar constriction by Aramine is an important action in maintaining the coronary circulation during cardiac tamponade.

In less severe tamponade, an elevation of filling pressure can still achieve a slight increase in diastolic fiber length. Under these circumstances, Aramine, by decreasing pressure-volume relationships of veins, might also contribute to its therapeutic benefit.

The experiments suggest that Aramine or other sympathomimetic agents which have both myocardial and vasoconstrictor actions may be of therapeutic value under these circumstances.

Summary and Conclusions

Simultaneous right and left ventricular function curves were done in 6 dogs to study the effect of Aramine and Wyamine on the heart and circulation during acute cardiac tamponade. Marked depression of the apparent right and left ventricular function curves occurred during tamponade. These curves were then significantly re-elevated by the administration of these 2 drugs. After the release of tamponade, post control curves were higher than the pretamponade curves. The increase in ventricular stroke work at any given filling pressure was independent of changes in pulse rate. In very severe tamponade, it is likely that an inadequate coronary perfusion gradient plays an important role because of the low aortic pressure and high right atrial pressure. An increase in peripheral vascular resistance produces a more adequate coronary perfusion pressure under these circumstances.

It is concluded that Aramine and Wyamine also augment myocardial contractility, thus inducing the heart to do more stroke work without requiring an increase in diastolic fiber length. These data suggest that in acute clinical tamponade, such drugs may be of value as a brief holding maneuver until such time as definitive therapy can be initiated.

Summario in Interlingua

Simultanee curvas de function dextero- e sinistro-ventricular eseva obtenite in sex canes pro studiar le effecto de Aramina e Wyamina super le corde e le circulation durante acute tamponamento cardiac. Marcate depressiones del apparente function dextero- e sinistro-ventricular eseva registrate durante le tamponamento. Le curvas se re-elevava significativemente sub le influentia del administration del duo drogas. Post le elimination del tamponamento, le curvas de controlo post-tamponamental eseva plus alte que le curvas de controlo pre-tamponamental. Le augmento del labor de pulso ventricular a omne pressiones de plenamento eseva independente de alterationes in le velocitate del pulso. In severissime formas de tamponamento, il es probable que inadequate gradientes de perfusion coronari ha un rolo importante a causa del basse pression aortic e del alte pression dextero-atrial. Un augmento del resistentia vascular peripheric produce sub iste conditiones un plus adequate pression de perfusion coronari.

Nos conclude que Aramina e Wyamina effectua etiam un augmento del contractibilitate myocardial de manera que le corde es inducite a augmentar su labor pulsatile sin que un augmento del longor del fibra diastolic es requirite. Iste datos suggere que in acute tamponamento clinico, drogas del typo mentionate pote esser de valor in le realisation de breve manovras retentori usque al tempore quando le therapia definitive pote esser initiate.

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Circ Res. 1956;4:705-709
doi: 10.1161/01.RES.4.6.705
Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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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:
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