Hemodynamic Parameters and Drug Action in Shock

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THERE are basically two schools of thought regarding the role of the heart in the development and progress of irreversible hemorrhagic shock. One indicates that cardiac failure occurs early in shock and may be the most responsible factor for the onset of irreversibility, the other suggests that peripheral vascular failure is the primary component of irreversible shock and cardiac failure is only a terminal factor. If a reduction in coronary blood flow during the period of hypotension with consequent myocardial damage is a causative factor in the development of irreversible shock, then, a pharmacologically induced coronary vasodilatation should prolong the hypotensive stress required to produce irreversibility. This possibility was investigated in the present study, and the results supported the contention that cardiac failure contributes to the development of irreversibility in shock. We have been working about the cardiac work in hemorrhagic shock.

Fig. 1 shows the block diagram of our data collection. The left chest was opened and Statham flow probe was attached at the tip of the aorta. Aortic pressure was measured by inserting a catheter via femoral artery, and then these signals were led directly to analogue computer. Thus we could get the ventricular work beat-by-beat continuously. Fig. 2 shows the recordings of parameters we took. We could get distinct tracing of parameters in case it is normotensive. As shown in Fig. 3, we could get the stroke ventricular work by the measurement of the height of each work profile. We accordingly applied this technic to determine the hemodynamic effects of various drugs in hemorrhagic shock. For instance, L.M.W.D., hydrocortisone, α -receptor stimulants, β -receptor stimulants, and blockers, and so on. The results of the experi-

ments are shown in Fig. 4 and Fig. 5. Fig. 4 shows the changes of left ventricular work treated with methylprednisolone in hemorrhagic shock. Fig. 5 shows the changes of left ventricular work treated with db-CAMP and Isoproterenol in hemorrhagic shock. Now we are wondering, we could get the good dose responses of the drugs in this way and not much information about the protective effects of them.

Fig. 6 shows the block diagram of the experiment. This time we used mongrel dogs divided into two groups; control group and Dipyridamole-treated group. As shown in Fig. 7, 0.15 mg/kg of body weight of Dipyridamole was infused at 5 minutes before bleeding, and a half dose of it at 30 minutes intervals during hypotension. A femoral artery was catheterized, and was connected to Statham pressure transducer to record arterial pressure at the ascending aorta, then to a computer and a research recorder of Electronics for Medicine to monitor the profile. The other femoral artery was catheterized and connected to a reservoir bottle to bleed. A tracheal tube was inserted and connected to an intermittent positive-pressure respirator. An incision was made through the fourth intercostal space on the left side. The base of the aorta was exposed and Statham's flow-probe was placed around it, then was connected to a flow meter and a computer. Two catheters were placed in the left atrium via the atrial appendage; one to measure mean atrial pressure, and the other to infuse the mixture of Hartman's solution and shed blood. Until mean arterial pressure was reduced to 35 mmHg, the dog was allowed to bleed rapidly into the reservoir. The reservoir was maintained at a constant pressure level of 35 mmHg. The volume of blood that each animal shed into the reservoir was recorded every 10

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Fig.1. Block diagram of data collection.

Fig.2. Recordings of left ventricular work with other parameters.

Fig.3.

minutes. After a variable period of time, each animal began to develop circulatory failure and became unable to maintain mean arterial pressure of 35 mmHg. Blood then began to flow from the

reservoir back into the dog. This occurrence was designated "reversal" and the period of time between the onset of hemorrhage and reversal was recorded in each experiment as a "reversal

Fig.4.

Fig.5.

Fig.6.

Fig.7.

Fig.8.

time". To make certain that the circulatory failure was progressive, each animal was observed till 40% of the shed blood had been taken back. After this manipulation, aortic pressure was raised up to 100 mmHg and maintained at this level for 2 hours by retransfusing the rest of the shed blood and Hartman's solution. From the aortic pressure and flow, left ventricular stroke work was obtained continuously. In the control group, mean reversal time was around 150 minutes; in the Dipyridamole-treated group, it was 170 minutes. The initial bleeding rate in two groups didn't show the significant difference.

However, Dipyridamole-treated dogs continued to bleed into the reservoir at a time when the control group had begun to take back blood. As for 40% reversal time, it was 235 ± 22.1 minutes in control group, and was 255 ± 22.1 minutes in Dipyridamole-treated group. It has been shown that the reversal and continued uptake of blood by an animal maintained at a constant hypotensive pressure is a good statistical indication that the animal has developed irreversible shock. It has been reported by West et al. that a dose of 0.2 mg/kg of body weight of Dipyridamole causes selective coronary vasodilatation. Its peak

Fig.9.

action is reached in about 5 minutes, and the duration of its action under normotensive condition is approximately 30 minutes.

To determine the ventricular function curve, the aortic pressure was lowered to 50 mmHg momentarily to keep aortic afterload constant. Hartman's solution was infused rapidly into the left atrium from the reservoir filled with approximately 250 ml. of it. Fig. 8 shows the relation between left atrial pressure and left ventricular stroke work. Aortic flow increased rapidly with the increase in left atrial pressure. The ventricular function curve was obtained 3 times; before the bleeding, at the time of 40% uptake and 2 hours later maintaining 100 mmHg aortic pressure. In control group, left ventricular function curves were depressed in order as control, hypotension and shock state. But in Dipyridamole-treated group, its function curves were depressed but not severe at the state of shock and sometimes showed a little recovering pattern. Sarnoff et al. demonstrated that cardiac deterioration during hemorrhagic hypotension could be reversed by augmenting coronary flow with external pump and others by a clamp to the ascending aorta. Meanwhile Elliot reported that coronary sinus flow was increased by Dipyridamole over a whole range of arterial pressure from normotensive conditions to shock levels. Jones et al. reported

significantly greater circumflex flow in dogs receiving Dipyridamole. These suggests protective effects of Dipyridamole during hypotension. These data imply that reduced coronary flow during hemorrhagic hypotension may contribute to the development of irreversibility in shock and the coronary vasodilatation induced pharmacologically during hypotension may have a protective effect.

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