Effect of Celiac Blockade and Dibenzyline on Traumatic Shock Following Release of Occluded Superior Mesenteric Artery *

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COMPLETE OCCLUSION of the superior mesenteric artery (S.M.A.O.) is lethal. In the experimental animal release of the occlusion after one or several hours hastens death, which is preceded by profound vascular collapse that is indistinguishable from traumatic shock caused by acute blood loss or by overwhelming infection. Occlusion of this vessel is, therefore, a convenient method for producing typical traumatic shock. The speed with which the shock develops and its severity depends on the duration of the occlusion. Antiadrenergic drugs can prevent death in this as in other types of experimental shock when given before shock has developed. But, like other effective prophylactic measures, they have little therapeutic value when given after shock has already developed.

Celiac blockade, another effective prophylactic measure, may have greater therapeutic potential than shown by antiadrenergic drugs. This is because selective release of vasoconstriction in the splanchnic area should divert more of the available peripheral flow to this area, which is the site of the critical lesion, than one would expect from the nonselective action of antiadrenergic drugs. This possibility has been studied.

Method

Experiments on Dogs

S.M.A.O. was performed under intravenous nembutal anesthesia in a series of 86 dogs by a technic described elsewhere.[8] The occlusion was released after 5 hours to ensure uniformly lethal shock in the untreated animal. Systemic arterial blood pressure was recorded continuously, beginning before occlusion and continuing for 2 hours after release.

Three methods of treatment were studied: 1) celiac blockade, 2) intravenous dibenzyline and 3) intra-aortic dibenzyline. Each method was applied with and without replacement of blood volume lost into the gut.

Lasting blockade of the celiac plexus was produced in 42 dogs by percutaneous injection of 25 cc. of 50 per cent ethyl alcohol in 0.5 per cent xylocaine into and around the celiac plexus. In 20 dogs the block was applied immediately before occlusion, in six at the middle of the 5-hour period of occlusion and in 16 immediately after release of occlusion. Of the 16, six received no additional treatment, while ten received fresh donor blood at frequent intervals for several hours to replace deficits, determined every half hour by a method described elsewhere,[9] as they occurred. In these ten dogs hypovolemia was thus excluded as a significant factor in the persistence of shock during the first few hours after resumption of flow.

Selective release of vasoconstriction in the splanchnic area was also attempted with dibenzyline in 16 dogs immediately after release of occlusion; 0.5 mg./Kg. in 5 ml. of saline was rapidly injected into the upper abdominal aorta at the level of T_{12} via a double-lumen 7F catheter, with a balloon 10 cm. from its tip inflated dur-

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TABLE 1. *Effect of Therapy for S.M.A.O. for 5 Hours in Dogs*

Type and Time of Therapy	No. Dogs	Survival—48 Hr.
No treatment	12	0
Saline injection into the celiac plexus	4	0
Blood volume therapy	6	0
Celiac blockade		
Before occlusion	20	12 (60%)
At middle of period of occlusion	6	4 (66%)
Shortly after release of occlusion		
With blood volume therapy	10	4 (40%)
Without blood volume therapy	6	0
Intra-aortic dibenzyline*		
Shortly after release of occlusion		
With blood volume therapy	10	5 (50%)
Without blood volume therapy	6	0
Intravenous dibenzyline**		
Shortly after release With blood volume therapy	6	1 (16%)

*0.5 mg./Kg. **1 mg./Kg.

ing the injection. Successful occlusion of the aorta during the injection was confirmed by disappearance of the femoral pulse. Of 16 dogs in this series, six received no blood volume therapy. In the other ten, hypovolemia was treated by transfusion, as described above, to avoid a significant deficit for the first 2 to 3 hours.

In another group of six dogs, 1 mg./Kg. of dibenzyline was injected into the femoral vein slowly (5 min.) to minimize its hypotensive effect. All six were monitored every 30 minutes for blood loss and given fresh blood from the beginning to reduce or prevent significant hypovolemia for 2 to 3 hours after release of the occlusion.

Control data to determine the value of blood volume therapy alone were also obtained. One group of 12 dogs received no treatment. A second group of four had 25 cc. of saline solution injected into and around the celiac plexus before occlusion. A third group of six received blood volume therapy only, sufficient to prevent significant hypovolemia for periods up to 2 hours after release of occlusion.

Experiments on Rabbits

The intestine of the dog is peculiarly vulnerable to injury from shock, so that the degree of hypovolemia from intestinal bleeding is itself sufficient to cause death.[5] This is not true in most experimental animals or in most patients with this disorder. Because severe hypovolemia does not occur in the rabbit, similar experiments were performed in this species to exclude this variable. All rabbits were put into S.M.A.O. shock by release of an occluding ligature around the S.M.A. 60 minutes after it had been applied under local anesthesia. Three methods of pretreatment were used: 1) celiac blockade by percutaneous injection of 1.5 ml. 50 per cent alcohol, containing 0.5 per cent xylocaine, into and around the celiac plexus;[6] 2) intravenous dibenzyline (1 mg./ml./Kg. body weight); and 3) intra-aortic dibenzyline at D10 in the same amount. The balloon technic was not used as in the dog. Treatment after release of the ligature was the same as in dogs: celiac blockade after 1, 15, 30 and 60 minutes, intravenous dibenzyline after 1 or 15 minutes, and intra-aortic dibenzyline after 1 or 15 minutes.

Results

Dogs (Table 1)

No Therapy. All 12 untreated dogs exhibited a similar response. Immediately after the artery was closed, the systemic arterial pressure rose about 20 mm. Hg and gradually returned to the preoccluded

level. On release of the ligature, a precipitous fall (average 25 mm. Hg) occurred. In most dogs pressure returned to normal in less than 15 minutes and then fell progressively until death which occurred within 18 hours in all experiments. The total blood lost into the gut during occlusion and the following 2 hours, measured in six dogs, ranged from 37 to 70 per cent (average 40%).

Blood Volume Therapy. The volume of blood required to keep pace with the loss within the first hour or two usually equalled 40 per cent of the normal volume. Although normovolemia was sustained for a while, hematocrit rose steadily to a level of 75. Therefore more plasma than red blood cells was being lost. Intraintestinal bleeding was relentless, and the blood volume therapy was discontinued after 90 minutes. Hypovolemia recurred subsequently. The only benefit from the transfusion was a transient pressor response of 30 to 60 minutes' duration. All six dogs in this group died.

Celiac Blockade Before Occlusion. Twelve of 20 dogs so treated survived. Five were monitored for total blood loss up to 2 hours after release of occlusion. This loss did not exceed 10 per cent. Since these five dogs were among the 12 survivors, and none of the 12 went into shock, it is assumed that the blood loss in all 12 was of this order. None of the survivors exhibited a bloody diarrhea.

Celiac Blockade During Occlusion (no blood volume therapy). Of six dogs blocked for 2½ hours before release of occlusion, four survived. Some of these four showed bloody diarrhea after release.

Celiac Blockade After Release. All six dogs so treated that received no additional therapy died. Of ten dogs so treated that also received blood immediately after release, sufficient to restore and sustain normovolemia for 1½ hours, only four survived. Average blood loss in this group of ten dogs was about 40 per cent—13 per cent during the period of occlusion and 27 per cent during the 2 hours after release. Blood loss in survivors was equal to that of the six that died.

TABLE 2. *Effect of Therapy for S.M.A.O. for 1 Hour in Rabbits*

Type and Time of Therapy	No. Rabbits	Survival—48 Hr.
No treatment	12	0 (0%)
Celiac blockade before occlusion	12	7 (60%)
Intra-aortic dibenzyline (1 mg./Kg.) before occlusion	12	6 (50%)
Dibenzyline (1 mg./Kg.) I.V. before occlusion	12	6 (50%)
Celiac Blockade		
1 min. after release of occlusion	12	5 (42%)
15 min. after release of occlusion	12	4 (33%)
30 min. after release of occlusion	12	4 (33%)
60 min. after release of occlusion	12	1 (8%)
Intra-aortic dibenzyline (1 mg./Kg.)		
1 min. after release of occlusion	12	4 (33%)
15 min. after release of occlusion	12	1 (8%)
Intravenous dibenzyline		
After 1 min.	8	0 (0%)
After 15 min.	8	0 (0%)

Intra-aortic Dibenzyline Immediately After Release. All six dogs so treated that received no additional therapy died. The time when shock developed, the degree of blood loss and the survival time were the same as in the untreated group. Of ten dogs receiving intra-aortic dibenzyline and blood sufficient to replace the loss during the first 2 hours, eight survived for the first 24 hours, but only five survived permanently. In those that died the onset of

shock was slower than in dogs receiving either dibenzyline alone or blood volume alone. Blood deficit after the first 2 hours following release was 40 per cent, of which 10 per cent was lost before release.

Intravenous Dibenzyline Immediately After Release. Of six dogs so treated together with replacement of blood lost during the first 2 hours, only one dog, which did not go into shock, survived.

Rabbits (Table 2)

Blood volume was monitored in ten control animals up to 1 hour after release. Values ranged from 95 to 107 per cent of normal. In a previous study, blood volume data obtained frequently until death showed that hypovolemia was not severe enough to explain the death.

All untreated animals died. Fifty to 60 per cent survived as a result of pretreatment by all three methods. Treatment at two intervals after release (1 min. and 15 min.) with intravenous dibenzyline was ineffective. Treatment with intra-aortic dibenzyline was of some benefit if given within the first minute, but not if given after 15 minutes. Celiac blockade was distinctly superior to intra-aortic dibenzyline because it was of some benefit (33% survival) when given as late as 30 minutes after release.

Therapy after 1 hour was useless in all three methods.

Discussion

Data in Tables 1 and 2 confirm previous reports showing that, in traumatic shock, prophylactic elimination of vasoconstrictor activity in the splanchnic area by celiac blockade is as effective as antiadrenergic agents given intravenously.[6] These data show also that considerable protection can be obtained if vasoconstriction in the splanchnic area is abolished very soon after release of the occlusion. Therefore, it appears that release of occlusion does not restore optimal flow and that if better flow can be provided early, the injury may still be reversible.

Since dibenzyline injected into the upper abdominal aorta of dogs early after release is about as effective as celiac blockade, whereas twice as much dibenzyline intravenously is of no value, the latter does not protect because it does not achieve a sufficient concentration at the site which is most in need of better flow.

The data also show that occlusion does not produce the same degree of injury in all animals, since release of vasoconstriction before or during occlusion protects only 50 to 60 per cent. Hence, collateral flow was less than adequate in the remainder.* This inference also follows from the failure to prevent the decline and death of more than 30 to 40 per cent of animals by regional antiadrenergic therapy instituted soon after release of the occlusion.

The development of typical traumatic shock so rapidly after release signifies flooding of the circulation with a vasocontrictor toxin that has accumulated in the gut wall during the period of occlusion. This toxin cannot be destroyed after release of occlusion in more than half the animals because their livers have lost the required detoxifying capacity. What remains of this detoxifying function in those that can be salvaged is so vulnerable that therapy is useless if it is withheld for more than half an hour.

There is evidence that shock after release of occlusion is a form of endotoxic shock: 1) Blood from animals in S.M.A.O. shock induces lethal shock in test recipients that is indistinguishable from endotoxic shock and is positive for endotoxin by several bioassay tests; [3] 2) in animals surviving as a result of prophylactic orally administered non-absorbable antibiotics the blood is negative for endotoxin by these

* This is not because of technical failure of the blockade, since blockade by injection under direct vision is not much more effective.

tests.[2, 10] This observation demonstrates that the intestine is the source of the toxin. The mechanism by which the endotoxin produces vascular collapse is described elsewhere.[3, 6, 7]

This explanation for the state of shock is preferable to one which attributes the shock to intestinal injury and the resulting hypovolemia from mucosal bleeding, because, as stated, shock in the dog is not less severe even while normovolemia is being maintained, and because the process is as lethal in the rabbit, which does not develop a significant hypovolemia.[3]

The foregoing analysis appears to be valid for the clinical analog of the experimental disorder. The literature records 13 recoveries after more than 200 operations for occlusion of the superior mesenteric artery.[1, 4, 5] Surgical release of the acute occlusion in man, as in the animal, usually fails, presumably because it accelerates vascular collapse, unless the occlusion is of very short duration. Experimental data suggest that any effort to release the occlusion should be preceded and supplemented by celiac blockade with replacement of measured deficits of blood volume, perhaps combined with intraintestinal antibiotics to suppress further bacterial activity.

Summary and Conclusion

Release of the superior mesenteric artery occluded for 5 hours in the dog produces profound and rapidly fatal traumatic shock. Severe loss of blood into the intestine begins soon after release and continues for hours afterward, reaching about 40 per cent of blood volume within 3 hours. Although this itself is lethal, full replacement of the measured loss does not prevent shock or death. Hence, there is an even more serious injury produced by ischemia. Because of evidence from previous studies that a lethal endotoxemia develops, the damage is not only to the intestine but also to the endotoxin-detoxifying potential in the liver.

In the rabbit occlusion of this vessel for 1 hour is sufficient to produce uniformly fatal shock; the pattern is like that in the dog except that blood loss into the gut is insignificant. With hypovolemia not exceeding 10 per cent, and the presence of lethal endotoxemia, as in the dog, the primary injury in both species is to the detoxifying system in the liver.

In previous studies in the rabbit, shock and death were prevented in 60 per cent of animals by prophylactic use of orally administered non-absorbable antibiotics or intravenous dibenamine. Present data confirm the prophylactic value of intravenous dibenamine and show that prophylactic release of vasoconstriction by celiac blockade or intra-aortic dibenzyline is also protective. Celiac blockade appears to be useful even when instituted halfway through the period of occlusion.

Results of therapy applied after restoring flow are not as good. Intravenous dibenzyline is of no value. Regional release of vasoconstriction by intra-aortic dibenzyline is useless unless given immediately after release. Celiac blockade can salvage one third of the animals when given up to 30 minutes after release.

In the dog, results are similar. Therapy after restoring flow is even less effective, for it is useless unless given immediately, and the release of vasoconstriction must be combined with transfusions for maintenance of normovolemia for several hours. The data indicate that the splanchnic area is the one most in need of better flow and is better served by selective diversion than by over-all release of vasoconstriction.

Vascular collapse that occurs so soon after restoring flow signifies that the toxin entering the circulation is a vascular toxin and is able to inflict injury because the normal detoxifying power of the liver has been damaged or destroyed by occlusion.

Since the load of toxin entering after release is greater than the load entering before release, the portal vein is the major pathway of entry.

These studies indicate why surgical restoration of flow in the acutely occluded superior mesenteric artery in man is seldom successful. They suggest that sustained celiac blockade should be applied as soon as the diagnosis is suspected, in order to improve flow to the ischemic liver as well as to the intestine.

The possibility of diverting blood in the superior mesenteric vein to the spleen in an attempt to detoxify it before it returns to the portal vein is currently under investigation.

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